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Abstracts

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Hämatologie

H1

Clonal hematopoiesis in patients with cancer and its association with risk of thrombosis and prognosis of disease

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Introduction and Aim: Patients with cancer are at high risk for cardiovascular events, particularly venous and arterial thromboembolism (VTE/ATE). Clonal hematopoiesis (CH) has been identified as risk factor for cardiovascular diseases, but its impact on thrombosis risk in cancer patients remains unclear. Therefore, this study aimed to investigate the association between CH and cancer-associated VTE and ATE.

Material and Methods: This study was performed within the framework of the Vienna Cancer and Thrombosis Study (CATS), a prospective observational cohort study. Peripheral blood DNA samples collected at study inclusion were screened for CH-associated mutations.

Results: In this study, 967 patients (median [interquartile range, IQR] age: 61 years [50–68], 49.9% female) were followed for a median of 24 (IQR: 24–24) months. The three most common cancer types were lung (21.0%), brain (19.0%), and breast (16.4%), 787 (78.3%) had newly diagnosed cancer and 434 (44.9%) had stage IV disease. Fifty-two CH-associated variants were detected in 46 patients (4.8%), with DNMT3A (48.1%) and TP53 (17.3%) mutations being the most common. The presence of CH was not associated with VTE (adjusted SHR: 0.68, 95% CI: 0.21–2.19) or ATE risk (adjusted SHR: 1.08, 95% CI: 0.15–8.06). Laboratory parameters, inflammatory and hemostatic biomarkers did not differ according to CH carrier status. Patients with CH showed decreased overall-survival compared to those without CH (12-month survival [95% CI]: 58.7% [45.7–75.3] versus 73.4% [70.5–76.4], $p = 0.02$).

Conclusion: In this cancer patient cohort, presence of CH was not associated with increased VTE or ATE risk, though CH carriers had reduced overall survival.

Die mit Sternchen (*) markierten Autoren sind die korrespondierenden Autoren.

H2

Evaluation of the impact of natural products and chemicals on proliferation and survival of ALL cells

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Acute lymphoblastic leukemia (ALL) is a life-threatening hematopoietic malignancy characterized by clonal expansion of lymphatic progenitors in the bone marrow and peripheral blood. Despite intensive treatment regimens and use of targeted drugs many patients cannot be cured. Therefore, new therapeutic options need to be developed. In recent years, the potential role of natural products and chemicals as therapeutics in hematologic malignancies has attracted attention. However, the effects of natural substances on ALL cells have not been investigated so far. In this study, we analyzed the effects of 9 selected natural substances in lymphoblastic cell lines (Ph+: BV-173, NALM-1, TOM-1; Ph-: BL-41, RAMOS, RAJI, REH) using proliferation and apoptosis assays. We found that resveratrol and spermidine inhibit the proliferation of both Ph+ and Ph- ALL cells in a dose-dependent manner (IC_{50} values for Ph+ ALL cells: resveratrol: 5–50 µM, spermidine: 0.01–1 µM; Ph- ALL cells: resveratrol: 10–50 µM, spermidine: 0.1–10 µM). Moreover, we were able to show that resveratrol and spermidine induce apoptosis in all lymphoblastic cell lines tested. Furthermore, we found that resveratrol and spermidine cooperate with the BCR::ABL1 inhibitors ponatinib and asciminib in suppressing survival of Ph+ ALL cells. In summary, our data show that natural products and chemicals can suppress proliferation and viability of Ph+ and Ph- ALL cells. Additionally, the combination of natural products with BCR::ABL1 inhibitors exerted cooperative anti-leukemic effects in ALL cells. Whether these substances are also effective in vivo and in ALL patients remains to be determined.

H3

Inhibition of TYK2 holds intrinsic and immune-mediated therapeutic potential in ALK-negative Anaplastic Large Cell Lymphoma

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Introduction and Aims: Systemic Anaplastic Large Cell Lymphoma (ALCL) is an aggressive T-cell lymphoma, with half of the patients carrying the hallmark NPM-ALK fusion. Remarkably, ALCL patients without the NPM-ALK fusion have a worse prognosis and here the molecular drivers remain elusive. Since, we have previously demonstrated the importance of TYK2 in

transgenic ALCL mouse models we hereby propose the TYK2 inhibitor Deucravacitinib as therapeutic option in this class of patients.

Methods: RNA-Seq with ALCL cell lines; murine xenograft models for ALCL, ALK-; flow-cytometry: PI/Annexin V, PD-L1, CD163, CD86 expression; co-culture of ALCL cells and human macrophages.

Results: Only ALCL, ALK- cells responded to TYK2 inhibition with lower phospho-tyrosine STAT1/STAT3 levels and also displayed a significantly lower IC50 than ALCL, ALK+ cells. In line, we found that ALCL, ALK- patients had higher TYK2 expression, suggesting a higher TYK2 dependence. Consequently in a murine ALCL, ALK- xenograft model Deucravacitinib was able to strongly reduce tumor growth. Moreover, TYK2 inhibition led to reduced PD-L1 expression on tumor cells and reduced macrophage CD163 and PD-L1 expression in coculture systems, which prevents immune-evasion and reduces tumor support of macrophages. RNA-Seq and gene set analysis after TYK2 inhibition revealed compensatory activation of the mTORC1 pathway. Indeed, combined TYK2 and mTORC1 inhibition resulted in strongly synergistic viability reduction.

Conclusions: Among ALCL types systemic ALCL, ALK- has the worst prognosis. We propose TYK2 and mTORC1 dual-inhibition as novel synergistic treatment avenue, particularly in ALCL, ALK- patients. Moreover, TYK2 inhibition promotes reactivation of patient's anti-tumor immune response.

H4

Newtrophil approach – Inhibition of myeloperoxidase ameliorates murine acute Graft-versus-Host Diseas

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Acute Graft-versus-Host disease (aGvHD) still presents a challenging obstacle to the success of allogeneic hematopoietic stem cell transplantation (alloHSCT) in curing cancer. GvHD is predominantly mediated by allo-reactive donor T cells, but neutrophils have recently been identified as early key players in the initiation of aGvHD. In this study, we investigate the effects of specific inhibition of myeloperoxidase (MPO) through 4-aminobenzoic acid hydrazide (ABAH) on aGvHD development in an MHC-mismatched mouse model (C57BL6/N -> BALB/c).

Recipient BALB/c mice undergo total body irradiation prior to bone marrow transplantation and ABAH or vehicle are administered by intraperitoneal injection.

Here, we show that treatment with ABAH effectively reduces MPO activity in vivo and significantly improves survival in mice when treatment is started prior to transplantation. ABAH-treated mice present with decreased early serum levels of pro-inflammatory cytokines and liver enzymes as well as reduced bacterial translocation in the small intestine. T cell proliferation and activation are not directly affected by ABAH, whereas chemokine expression and T cell infiltration are decreased in target organs of ABAH-treated mice and correlate with reduced inflammation. Simultaneously, treatment with ABAH largely preserves the Graft-versus-Leukemia (GvL) effect and does not aggravate the risk for infection with E. coli bacteria.

In conclusion, our data suggest that inhibition of MPO ameliorates aGvHD severity and prolongs survival in mice. We propose that targeting neutrophils with ABAH allows the interception at the earliest stages in the initiation of aGvHD and could present a novel therapeutic strategy.

H5

Differential in vitro sensitivity of BCR::ABL1 kinase domain mutations to tyrosine kinase inhibitors depending on the p190 or p210 background

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Introduction and aim: The p210 and p190 BCR::ABL1 fusion protein isoforms represent the genetic drivers in Ph^+ leukemias and display differential signaling properties. Nevertheless, all previous in vitro studies assessing the responses of single and compound mutations in the BCR::ABL1 kinase domain (KD) to various tyrosine kinase inhibitors (TKIs) have only been performed in the background of the p210 variant, which is predominant in chronic myeloid leukemia (CML). Therefore, we addressed potentially relevant differences in TKI response in the p190-background, which is predominant in Ph^+ acute lymphoblastic leukemia (Ph^+ALL).

Method: In vitro testing of 67 different KD mutations in both backgrounds using Ba/F3 cells.

Results: Most TKIs showed < 3-fold differences in IC_{50}-values for identical mutations in the p210- and p190-background, while greater than 3-fold differences were observed for 12–29% of the mutations, depending on the TKI tested. Some of the differentially increased IC_{50}-values exceeded clinically achievable TKI concentrations, suggesting that the expected clinical responses might reveal relevant differences for individual mutations and TKIs. The most prominent differences were observed for asciminib revealing > 1000-fold higher IC50-values for specific mutations in the p210- versus p190-background. Examples include various compound mutations and the *P*-loop mutations E255V and Y253H, both highly resistant to asciminib in the p190-background.

Conclusion: Our observations indicate that the heatmaps for various mutations and TKIs in the p210-background will need to be supplemented by corresponding heatmaps established specifically for mutations occurring in the p190-background to support adequate TKI selection in the two most commonly occurring isoforms of the fusion gene.

H6

Triple drug treatment options for the highly resistant compound BCR::ABL1 mutation T315I/F359V in Ph-positive leukemia

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Introduction and aim: In Ph-positive acute lymphoblastic leukemia (Ph⁺ALL) and in advanced phases of chronic myeloid leukemia (CML), patients frequently develop compound mutations (CMs), defined as the presence of more than one mutation on the same BCR::ABL1 molecule in a leukemic cell. Many CMs are highly or even completely resistant to any individual tyrosine kinase inhibitor (TKI), including the 3rd-generation compounds ponatinib and asciminib. In a recent study, we demonstrated that CMs displaying high levels of resistance to all available TKIs applied as single agents, mostly revealed adequate in vitro responses to dual-drug combinations including ponatinib, most commonly coupled with asciminib, hydroxyurea or crizotinib (Am J Hematol. 2024,99(1):E9-E11). A major exception was the commonly observed CM T315I/F359V, against which no two-drug combination tested was effective. Therefore, we investigated whether a triple drug combination can overcome the resistance.

Method: Ba/F3 cells expressing BCR::ABL1 T315I/F359V were tested in vitro against ponatinib and two of the three most promising agents identified in our earlier studies including asciminib, hydroxyurea and crizotinib.

Results: The combinations of ponatinib with either asciminib and hydroxyurea, or with asciminib and crizotinib at low concentrations of all drugs effectively inhibited in vitro survival of the T315I/F359V mutant cells.

Conclusion: Since our earlier data indicated a good correlation between in vitro test results and clinical responses, our observations may provide a basis for novel treatment options with expectedly low toxicity in patients with CML or Ph⁺ALL displaying this (and conceivably also other) highly challenging BCR::ABL1 KD-mutation(s).

H7

Long-term survival of patients with relapsed/refractory acute leukemia after Clofarabine/Cyclophosphamide prior to stem cell transplantation

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Acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) are aggressive hematologic malignancies. In patients with refractory or relapsed (R/RR) disease allogeneic hematopoietic stem cell transplantation (HSCT) is the only potential curative procedure.

We retrospectively analyzed 82 patients (median age: 47.5 years; f:m ratio 1:1.28) with R/RR leukemia, treated with a debulking regimen of Clofarabine and Cyclophosphamide (ClofCy) as a bridge to HSCT. ClofCy resulted in a significant reduction in blood leukocytes and blast cells within five days. A median of 2 cycles were given. Treatment was well tolerated, only a few patients showed moderate liver toxicity (increase in aspartate-aminotransferase alanine-aminotransferase and alkaline-phosphatase).

Fifty-one patients (63%) proceeded to HSCT, in 31 (37%) infections, blast cell increase or clinical deterioration prevented HSCT. The median number of chemotherapies for R/RR leukemia prior to ClofCy was 2 (IQR 1–3) in patients eligible for HSCT and 3 (IQR 2–3) in those not eligible for HSCT. The number of chemotherapies administered for R/RR leukemia prior to ClofCy was a significant independent prognostic factor for proceeding to HSCT ($p = 0.004$). The median overall survival (OS) after HSCT was 1.23 years, with a 5- and 10-year survival rates of 38.4 and 31%, respectively. Chronic graft-versus-host disease (cGVHD) was associated with better OS and relapse-free survival (RFS). In contrast, acute GVHD predicted poorer outcomes ($p = 0.016$).

ClofCy is an effective debulking strategy for patients with R/RR leukemia prior to HSCT. According to our results, ClofCy should be introduced early to prevent repetitive intensive therapy.

H8

Teclistamab-Lenalidomide and Teclistamab alone vs Lenalidomide alone in newly diagnosed multiple myeloma as maintenance therapy following autologous stem cell transplantation: Phase 3 MajesTEC-4/EMN30 safety run-in

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Introduction and Aim: Teclistamab and lenalidomide (Tec-Len) may have synergistic antimyeloma effects. MajesTEC-4/EMN30 is a randomized, open-label, Phase 3 study evaluating Tec-Len maintenance in newly diagnosed multiple myeloma (NDMM) after induction and autologous stem cell transplantation (ASCT), ± consolidation. We report safety run-in results.

Materials and Methods: Patients with NDMM had received 4–6 cycles of induction therapy and achieved ≥ partial response. Three Tec dose frequencies were evaluated (Cohorts 1 and 2, Tec-Len; Cohort 3, Tec). Adverse events (AEs) were graded per CTCAE v5.0 (cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome per ASTCT). Investigator-assessed response was per IMWG 2016.

Results: Of 94 enrolled patients, 97% remained on treatment at median follow-up (4.9–14.4 months). Neutropenia and infections were the most common Grade 3/4 AEs. The cumulative incidence of any-grade and Grade 3/4 neutropenia showed a decreased trend with less frequent Tec dosing (69–37% and 66–28%, respectively), with a similar trend for all-grade infections (78–61%). In Cohort 1, all 28 patients with 12-month minimal residual disease (MRD) assessments had MRD-negative complete response (CR). All 10 MRD-positive patients and all 16 with <CR at study entry achieved MRD-negative CR and ≥CR, respectively. Efficacy in Cohorts 2 and 3 and longer-term Cohort 1 outcomes will be presented.

Conclusion: Tec-Len and Tec can be safely administered as maintenance therapy following ASCT in NDMM, with a trend for improved early safety outcomes with less frequent Tec dosing. Tec-Len demonstrated deepening responses. The randomized part of MajesTEC-4/EMN30 is actively enrolling.

H9

Concomitant TP53 and del(5)(q) aberrations in MDS and AML-MRC – a single center experience

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Deletion (5)(q) and TP53 mutations affect clinical course in MDS-related neoplasias. We retrospectively analysed clonal evolution and outcomes in patients with both del(5)(q) and TP53 mutations.

We identified 17 patients (median age: 65 years (95% CI, 38–80)) with MDS ($n=10$), t-AML ($n=2$), and AML-MRC ($n=5$). At the time of diagnosis, all patients had del(5)(q), and 14/15 patients had at least one TP53 mutation (7 monoallelic, 7 biallelic). Eleven patients had comutations, and in 14/17 patients, del(5)(q) was part of a complex karyotype. Among patients with genetic follow-up data, 8/10 patients showed an increase in TP53 VAF, 3 developed an additional TP53 mutation, and 1 remained stable. A slightly higher mean VAF was observed in patients with AML-MRC.

The median overall survival (OS) for all patients was 1277 years (95% CI, 0.725–1829 years). For patients with del(5)(q) and a monoallelic TP53 mutation, the median OS was 1501 years (95% CI, 1064–1939 years), whereas it was 1197 years (95% CI, 0.335–2059 years) for those with del(5)(q) and biallelic TP53 mutation. Among transplanted patients ($n=6$), median OS was 1277 years (95% CI, 1111–1442 years). Only 1 patient with isolated del(5)(q) and a progressing but still monoallelic TP53 mutation was a long-term survivor (52+ months).

We confirm that concurrent del(5)(q) and TP53 mutations, especially biallelic TP53 or complex karyotypes, result in poor prognosis. As effective treatment for biallelic TP53 mutant disease remains lacking, monitoring for clonal evolution is crucial to initiate early treatment.

H10

Optimizing Belantamab mafodotin in triple-class refractory multiple myeloma: impact of dose modifications on keratopathy incidence in a real-world retrospective study

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Introduction and Aims: Belantamab mafodotin (Belamaf) is a BCMA-targeting antibody-drug conjugate for treating triple-class refractory multiple myeloma. Although effective, keratopathy is a common dose-limiting side effect. In November 2022, GSK withdrew Belamaf from the U. S. market due to unmet confirmatory trial requirements, impacting its availability in Austria outside clinical trials or compassionate use.

This study aims to characterize the cohort, identify predictors of response, and assess dose modification effects on keratopathy.

Materials and Methods: In this retrospective study, 36 patients treated with Belamaf at the University Hospital of Vienna between January 2020 and June 2024 were assessed, with 42% receiving a reduced dose of 1.9 mg/kg.

Results: An overall response (≥ partial response) was observed in 64% of patients (CR:22%; VGPR:25%; PR:17%), with responders having significantly fewer prior therapy lines (median 3) than non-responders (median 4.5, $p=0.015$). Keratopathy occurred in 75% of patients, with 19% experiencing grade 4 and 14% experiencing grade 3 keratopathy. The median time to first vision impairment was 41 days. Patients receiving all cycles at a reduced dose (1.9 mg/kg) showed significantly lower rates of severe keratopathy (grade 3/4) compared to those on the full dose (2.5 mg/kg) ($p=0.004$). Importantly, dose reduction did not adversely affect progression-free survival or overall survival.

Conclusion: In real-world use, Belamaf demonstrates substantial efficacy in heavily pretreated multiple myeloma patients, with fewer prior therapy lines being predictive of response. Dose reduction to 1.9 mg/kg may mitigate severe keratopathy without compromising efficacy, suggesting a viable strategy to improve tolerability in clinical practice.

H11

Impairment of renal function in patients with Ph+ CML receiving imatinib

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Introduction and Aims: Tyrosine kinase inhibitors, applied as long-term therapy have significantly improved survival in patients with chronic myeloid leukemia (CML). Considering

long-term application, monitoring of potential organ toxicities including the renal function is of importance.

Material and Methods: We retrospectively analyzed the renal function in 229 CML patients (median age: 54 years; range: 12–86 years) treated with imatinib between 2000 and 2020.

Results: At diagnosis, median serum creatinine (Crea) was 1.0 mg/dL (range: 0.5–1.51 mg/dL). Only patients with arteriosclerosis had significantly higher Crea levels ($p<0.05$). In the entire cohort, a significant increase of Crea was observed within the first years after initiation of imatinib ($p<0.05$). This significant increase was observed in patients with an initial Crea≤1 mg/dL and those with Crea>1 mg/dL. We next analyzed the increase in Crea levels in different age groups (<36 years, 36–55 years, 56–65 years, >65 years). A significant increase in Crea was observed in patients aged 36–55 years ($n=73$; $p<0.05$) and 56–65 years ($n=66$; $p<0.05$), whereas the increase in patients aged <36 years was not significant and no increase in Crea was observed in those >65 years ($n=47$). In a subset of patients ($n=34$), a marked Crea increase was found (2 required hemodialysis). The overall survival did not differ between patients with a markedly increase in Crea (>0.5 mg/dL) and those with stable Crea.

Conclusion: Long-term treatment of CML patients with imatinib may be associated with impairment of kidney function. Thus, continuous monitoring of kidney function is recommended in all CML patients.

H12

Transcription factor STAT1 activation using molecular degrader-drugs as anti-lymphoma strategy in ALCL

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Introduction and Aim: Anaplastic large cell lymphoma (ALCL) is an aggressive, CD30+ T-cell lymphoma with 50% of patients bearing the typical NPM-ALK fusion. The JAK/STAT signaling pathway is highly active in ALCL and STAT3 and STAT5 are described as tumor promoters. In contrast, the role of STAT1 in ALCL is less clear.

Materials and Methods: Transgenic ALCL mouse model with and without STAT1 abrogation; Immunohistochemistry on ALCL patient tissues; resazurin assay, Annexin V/PI staining using flow cytometry, PTPN1/2 phosphatase inhibitor (ABBV-CLS-484) and PROTAC degrader DU-14; ALCL cells with and without CRISPR-mediated STAT1 knockout; Immuno-blotting; murine xenograft models of ALCL, ALK+.

Results: We observed high levels of STAT1 Tyr701 phosphorylation in ALCL patient tissues, raising the question of its role in lymphomagenesis. To clarify this, we have created a STAT1 knockout in the established CD4-NPM-ALK mouse model. We saw strongly reduced overall survival in the STAT1-/- mice indicating that STAT1 is a tumor suppressor. Surprisingly, in ALCL, ALK+ cells the PTPN1/2 degrader DU-14 was able to induce apoptosis, through hyper-activation of STAT1 and NPM-ALK. Consequently, STAT1-knockout cells were more resistant to DU-14. Finally, in a murine xenograft ALCL, ALK+ model DU-14 treatment led to complete abrogation of tumor growth. Immunohistochemistry staining of the tumors showed PTPN1/N2 degradation and activation of STAT1 Tyr701 phosphorylation along with caspase-3 cleavage in the treated tumors.

Conclusions: Paradoxically, activation of the JAK-STAT pathway by phosphatase degrader drugs leads to STAT1 and ALK-dependent cell death in ALCL cells and tumor abrogation in murine ALCL, ALK+ mouse models.

H13

Antiphospholipid antibody positivity in a large cohort of adult primary ITP patients: results from the Vienna ITP Biobank

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Introduction: Primary immune thrombocytopenia (ITP) is associated with bleeding but also a paradox thrombotic risk. Antiphospholipid antibody (aPL) positivity has been reported in ITP.

Method: The Vienna ITP Biobank is an ongoing prospective cohort study, recruiting adults with primary ITP at 2 tertiary care centers. Overall study design has been described in detail in previous publications.

Positivity for lupus anticoagulant (LA) and/or antibodies against cardiolipin (aCL) and/or β_2 glycoprotein I (aβ2GPI) was analyzed and associated with previous thrombotic events and bleeding severity, assessed using the ITP ISTH SMOG.

Results: 180 patients with primary ITP, of them 111 female, were analysed. Mean age was 50 years; median platelet count was 62 G/L. 25 patients (13.9%) had a history of TE.

27 patients (15.0%) were classified as aPL positive (12 single-, 10 double-, 5 tripple-positive), most commonly with aCL IgM. 5 aPL positive patients had a history of TE, which did not differ significantly from aPL negative patients. aPL positive ITP patients did not differ significantly in other clinical or laboratory parameters, such as platelet count, treatment history, or bleeding scores.

aPL positivity was significantly associated with age in uni- and multivariable logistic regression. Neither aPL positivity, nor degree of aPL positivity was associated with history of TE or bleeding severity.

Conclusion: While aPL positivity was associated with age, it did not significantly impact clinical characteristics or the risk of thrombotic events in our ITP cohort. Larger studies are needed to further assess the risk of thrombosis in ITP patients with aPL.

H14

CDK6 together with HDACs dictates maturation, immunogenicity and survival of FLT3 mutant AML

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Over 30% of patients with AML harbor oncogenic FLT3 mutations. FLT3 inhibition is not curative, illustrating the need for more effective pharmaceuticals.

We have recently demonstrated hypersensitivity of $FLT3^{mut}$ AML to the CDK4/6 kinase inhibitor palbociclib. The toxicity is ascribed to the transcriptional activity of CDK6 -a feature not shared by CDK4- on FLT3 and other oncogenes that mutant cells are addicted to.

Here, we aimed to identify new combinations of interest with palbociclib that could help AML patients to achieve maximum disease control; and to analyze genetic and cellular network determinants of synergism.

We discovered a pronounced synergy between palbociclib and the oral HDAC inhibitor chidamide at low nanomolar range. Such toxicity was specific for $FLT3^{mut}$ cells as $FLT3^{WT}$ cells failed to respond to the combination. Dually inhibited $FLT3^{mut}$ cells were accumulated in the sub-G1 compartment of cell cycle. This toxicity was due to induction of apoptosis. Selective CDK6 degradation mimicked the effects of palbociclib. Targeting CDK6/HDACs stimulated interferon signaling and enhanced antitumor immunity by overcoming a central mechanism of tumor immune evasion: it induced the efficiency of tumor cell antigen presentation via MHC class I. The treatment thus converts AML from cold to hot state, and provides rationale for combination with immunotherapies. Dually inhibited $FLT3^{mut}$ cells displayed a more mature phenotype with increased CD86. Hence, AML cells are reliant on HDACs and CDK6 to maintain immature phenotype and dual treatment provides a good alternative for treatment especially for those not suitable for chemotherapy.

H15

Die CAR-T-Zell Expansion als prognostische Marker für das Ansprechen auf CAR-T-Zelltherapie bei Non-Hodgkin-Lymphomen und Akuter Lymphatischer Leukämie

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Einleitung und Fragestellung: Kommerziell verfügbare chimäre Antigen Rezeptor (CAR)-T-Zellen (CARTs) enthalten eine kostimulatorische Domäne (2G.CARTs), CARTs der 3. Generation (3G.CARTs) zwei kostimulatorische Domänen. Diese Arbeit untersuchte 2G.CARTs und eigenhergestellte 3G.CARTs (HD-CAR-1) bezüglich der CARTs-Expansion im Zusammenhang mit dem klinischen Verlauf der Patienten.

Patienten und Methoden: Die retrospektive Kohorte von 76 Patienten wurde mittels CAR-T-Zell-Therapie am Universitätsklinikum Heidelberg therapiert. Gruppen (G) wurden nach Diagnosen und CARTs Generationen gebildet: G1 ($n=13$): Akute lymphatische Leukämie, 3G.CARTs (HD-CAR-1); G2 ($n=19$): Chronisch lymphatische Leukämie und Non-Hodgkin Lymphom (NHL), 3G.CARTs (HD-CAR-1); G3 ($n=10$): NHL, 2G.CARTs (Tisagenlecleucel); G4 ($n=34$): NHL, 2G.CARTs (Axicabtagene Ciloleucel). CARTs wurden mittels quantitativer Polymerase-Kettenreaktion ermittelt und der CARTs Spitzenwert (C_{max}) errechnet. Einteilung nach medianer C_{max} in strong-/weak expander (SE/WE) und anschließende Korrelation der Expansion mit: Therapieansprechen an Tag 90 nach CART, Nebenwirkungen, Gesamtüberleben.

Ergebnisse: G2 erreichte die höchsten medianen C_{max} Werte bis Tag 28 nach CART (37.226*), gefolgt von G4 (24.596*), G1 (22.375*) und G3 (18.623*) *[CAR copy number/µg PBMC DNA]. Bestes Therapieansprechen zeigte sich durch die höchste ORR (overall response rate: komplette Remission oder partielle Remission) bei den SE in G2 (78 %) gefolgt von G1 (67 %), G3 (67 %), G4 (50 %). 3G.CARTs SE zeigten mit 76 % eine überlegene ORR gegenüber der ORR von 50 % bei 2G.CARTs SE. Die Nebenwirkung CRS (Zytokin Freisetzungs-Syndrom) war bei 3G.CARTs seltener (G1: 23 %, G2: 53 %) als bei 2G.CARTs (G3: 70 %, G4: 79 %). CRS trat bei NHL 3G.CARTs bei höherem medianen C_{max} (86.960*) auf als bei 2G.CARTs (G3: 27.579*, G4: 49.710*). In G1 und G2 trat kein ICANS (Immuneffektorzell-assoziiertes Neurotoxizitätssyndrom) auf, in G3 bei 10 %, in G4 bei 79 %. Insgesamt 10 % höhere Überlebenswahrscheinlichkeiten wurden bei 3G.CARTs beobachtet. Dabei zeigen SE im 1-Jahres-Überleben bessere Werte (SE:WE): G1 (86 %:42 %), G2 (86 %:45 %), G3 (80 %:60 %), G4 (76 %:82 %);

Schlussfolgerungen: 3G.CARTs zeigen gegenüber 2G.CARTs überlegene Ergebnisse: höhere Expansion, verbessertes Therapieansprechen, reduzierte Nebenwirkungen (kein ICANS) und signifikant (G2 SE) besseres Gesamtüberleben. C_{max} bis Tag 28 korrelierte mit dem Therapieansprechen und eignet sich als prognostischer Marker.

Onkologie

O1

First-line somatostatin analog therapy in small intestinal and pancreatic neuroendocrine tumors: real-world data from a single center

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Background: Somatostatin analogs (SSA) are commonly used as a first-line therapy in slowly growing neuroendocrine tumors (NET) of enteropancreatic origin. Real-world treatment outcomes are of interest.

Methods: This monocentric retrospective analysis assessed progression-free survival (PFS) and overall survival (OS) in a subset of patients with small intestinal (si-) or pancreatic (pan-) NET grade 1 or 2 and first-line palliative SSA treatment at the Medical University of Vienna.

Results: In total, 96 patients were included, two-thirds of whom had a si-NET ($n=65$) and one-third a pan-NET ($n=31$). At diagnosis, the median age was 64 years, 60% were male, 94%

had ECOG 0, and 82% had stage IV disease. Overall, 34% had a NET G1, 55% NET G2, and 10% NET G1/G2 unclassified, with the median Ki-67 index being 4.0% (range: 0.5–19.0%). All patients tested were somatostatin receptor-positive (by functional imaging or immunohistochemistry). Lanreotide autogel was administered in 66% of patients (81% of pan-NET) and octreotide LAR in 34% (42% of si-NET). The median real-world PFS was 37.7 months (95% CI: 26.4–51.5) overall, 23.2 months (95% CI: 8.0–64.2) for pan-NET, and 39.3 months (95% CI: 32.2–68.2) for si-NET. The PFS differed significantly ($p=0.002$) between NET G1 and NET G2 (median PFS of 59.3 versus 26.4 months). There was no PFS difference between lanreotide and octreotide (37.6 versus 37.7 months). The median OS from treatment start was 93.5 months.

Conclusion: These data highlight the long periods of disease stabilization that can be seen with SSA in enteropancreatic NET.

O2

XPO1 in pancreatic cancer: novel biomarker insights and therapeutic innovations

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Introduction & Aim: Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive malignancy with poor survival rates. Exportin-1 (XPO1), a key nuclear export protein, is frequently overexpressed in various cancers, where it facilitates the nuclear export and subsequent inactivation of tumor suppressor proteins. Our study aims to evaluate the biological and prognostic role of XPO1 in PDACs.

Materials & Methods: We analyzed transcriptomic data from 12 public datasets, compiling the largest PDAC cohort to date with 1972 patients. Patients were stratified into tertiles based on XPO1 mRNA expression levels, and survival outcomes were assessed. To investigate functional roles, we used a CRISPR-Cas9 system to establish inducible XPO1 knockout PDAC cell lines and performed cell proliferation assays. Additionally, single-cell RNA sequencing (scRNA-seq, BD Rhapsody) was conducted on untreated PDAC tissue samples ($n=3$) to assess cell-type-specific expression.

Results: Transcriptomic analysis revealed a significant upregulation of XPO1 in PDAC tissues compared to healthy tissue, correlating with reduced overall survival. Bioinformatical analyses revealed significant differences in a high number of various pathways (i. e. MAPK signaling) between $XPO1^{high}$ and $XPO1^{low}$ PDACs. Functional studies showed that XPO1 knockout led to a marked decrease in cell proliferation. Preliminary scRNA-seq data indicated elevated XPO1 expression in epithelial cells and macrophages within the tumor microenvironment.

Conclusion: We have established the largest PDAC dataset to date, demonstrating that high XPO1 expression is linked to poor prognosis. The reduction in cell proliferation upon XPO1 knockout underscores its potential as a therapeutic target. Ongoing studies will further clarify XPO1's role in PDAC biology.

O3

MSI-H/dMMR solid tumors in Austria: a retrospective cohort study in four academic centers

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Introduction and Aims: MSI-H/dMMR (microsatellite instability high/deficient mismatch repair) is an important biomarker in various solid tumors. This retrospective analysis summarizes data from four academic centers in Austria, encompassing colorectal, gastric, small bowel, endometrial, ovarian and biliary cancer. Its primary aim was to report on MSI/MMR testing rates and modalities as well as the occurrence of MSI-H/dMMR in these tumor types.

Results: In sum, data on 3804 patients diagnosed between 2012 and 2020 was collected. Endometrial cancer patients were most likely to be tested (47.2%, 183/388), followed by colorectal (40.2%, 824/2052), small bowel (15.5%, 9/58), gastric (9.9%, 90/907), biliary (7.7%, 7/91), and ovarian cancer (1.3%, 4/308). The most frequently used method was IHC (69.0%), then PCR (15.9%) and the combination of multiple approaches (15.1%). Overall, 16.8% (188/1117) of the patients tested for MSI-H/dMMR had a positive result.

Additional data on a subset of colorectal ($n=90$) and endometrial cancer patients ($n=30$) with confirmed MSI-H/dMMR tumors was collected. Here, we recorded initial and subsequent therapy and provide information on additional molecular testing.

Conclusions: Overall, this chart review showed high testing rates in Austria for colorectal and endometrial cancer—before 2020 and previous to any approval of immune checkpoint inhibitors in any of these tumor types. Hence, current practice is unlikely to be reflected correctly by this dataset. According to up-to-date guidelines, MSI/MMR testing should be performed whenever these tests may identify suitable therapies.

O4

Systemische Inflammation fördert die Kachexieentwicklung bei PatientInnen mit Pankreaskarzinom

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Introduction: Cancer associated cachexia is a common phenomenon in patients with pancreatic cancer (PC) limiting patients quality of life and the ability to receive systemic therapy.

Material and Methods: Patients with PC diagnosed and treated at the Medical University of Vienna between 1999 and 2020 were identified through our PC database. The occurrence of cancer cachexia (CC) as well as clinical characteristics and outcome data were assessed via retrospective chart review. CC was defined according to the ESMO clinical practice guidelines as weight loss >5 or 2% if BMI<20 and concomitant systemic inflammation (defined as a modified Glasgow Prognostic Score (mGPS)>0).

Results: Among 747 PC patients included in the study, no association between weight at PC diagnosis and survival were observed ($p>0.05$), while the presence of systemic inflammation was associated with a 1.56-fold risk increase for death (95% CI 1.27–1.91, $p<0.001$). CC occurred in 97 (39%) of 329 patients 2–6 months after PC diagnosis and was associated with an impeded survival (HR: 1.8, 95% 1.41–2.46, $p<0.001$). In a multivariable analysis, only the presence of systemic inflammation was negatively linked to survival with a HR of 1.91 (95% CI: 1.41–2.59, $p<0.001$), while weight loss did not show any associations ($p>0.05$).

Conclusions: The occurrence of CC represents a frequent complication in PC and is associated with an impaired outcome. Systemic inflammation seems to be an important driver and therefore warrants further translational research to understand the pathophysiological background.

O5

Pyridostatin increases tumor immune cell infiltration and sensibilizes tumors for checkpoint therapy

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Introduction & Aims: In the past decade, checkpoint blockade has revolutionized cancer therapy. Though many patients show improved long-term survival after checkpoint blockade, even in well responding tumor entities about 50% of treated tumors do not respond or develop resistance. One key feature of non-responding tumors is being immunologically "cold", meaning they only contain a small number of tumor-suppressing lymphocytes.

In this study, we injected Pyridostatin (PDS), a small molecule that binds secondary DNA structures called G-quadruplexes, intratumorally in B16-OVA tumor-bearing mice, aiming to increase tumor immune cell infiltration and initiating an anti-tumor T cell response.

Material and Methods: We used the checkpoint therapy resistant B16OVA and Hcmel3 melanoma models to analyze tumor growth and survival. We dissected tumor immune cell infiltration through spectral cytometry and single cell RNA sequencing. Additionally, we analyzed the direct effect of PDS on different immune cells both in vitro and in vivo.

Results: Following intratumoral injection of PDS, we observed significantly decreased tumor growth, prolonged survival and successful checkpoint blockade. This effect was driven by the activation of myeloid cells, leading to increased levels of pro-inflammatory chemokines/cytokines followed by significantly increased infiltration of NK and cytotoxic T cells (CTLs) on day nine post-treatment. We also observed that infiltrating NK cells and CTLs of PDS-treated tumors produced significantly more Granzyme B.

Conclusion: In sum, our results suggest that G-quadruplex stabilization via PDS treatment harbors the potential to induce intratumoral inflammation and sensitize non-responding tumors for checkpoint blockade.

O6

Metabolic ketoacidosis as a severe complication of Enfortumab-vedotin/Pembrolizumab in metastatic urothelial carcinoma

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Background: Enfortumab-vedotin (EV) in combination with pembrolizumab (Pem) is the standard of care in the 1st-line therapy of advanced urothelial carcinoma (UC). EV/Pem is generally associated with less overall toxicity than platinum-based chemotherapy, new side effects are challenging and become severe in rare cases. In this case report we present a patient with fatal diabetic ketoacidosis.

Case presentation: A 60-year-old male patient was diagnosed with UC in 2022. After neoadjuvant chemotherapy a cystectomy was performed, followed by adjuvant immunotherapy until 01/24. Pulmonary recurrence was diagnosed in 08/2024. 1st-line therapy with EV/Pem was started. After two EV doses, the patient was hospitalized due to hyperglycaemic derailment with ketoacidosis. Despite extensive fluid substitution and insulin doses of up to 14 international units per hour (IU/h), the metabolic situation worsened with increasing lactate levels. The patient was transferred to the intensive care unit on day 2, where insulin doses of up to 40 IU/h were administered. Hemodialysis was necessary to keep the acid-alkaline balance in check. The patient died after four days of intensive care.

Conclusions: As to our knowledge, only five cases of EV induced fatal ketoacidosis were reported worldwide. In almost all of these cases, the clinical course, with an ultimately fatal outcome, mimic our patient. So far, there are only assumptions on the pathogenic mechanisms that lead to the apparent absolute insulin resistance. Treating physicians need to be aware of this adverse event and be cautious when treating patients with high BMI and/or uncontrolled diabetes.

O7

Demonstration of immunotherapy-induced changes in immune cell activation in a primary Patient-derived Micro-Tumor model (PMT)

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Introduction: While immunotherapy (IO) has led to significant therapeutic advancements, variability in patient responses remains a major challenge in oncology. To address this, we developed a functional 3D in vitro platform using primary tumor tissue, enabling personalized therapy testing and enhancing the accuracy of outcome predictions in a clinically meaningful way.

Material and Methods: Tumor samples from 30 NSCLC patients were processed into single-cell suspensions and seeded in ultra-low attachment plates. After six days, PMTs were treated with checkpoint inhibitors (CPIs) alone and with chemotherapies. Drug response was tracked by size changes using bright-field imaging. Additionally, supernatant was collected to conduct an ELISA assay for monitoring cytokine release. T-cell activation in response to therapy was further analyzed via FACS. Furthermore, Immunohistochemistry (IHC) and RNA Bulk Sequencing have been performed for further validation.

Results: In terms of PMTs size regression during treatment (reflecting tumor shrinkage), the model's objective response rates closely align with the distribution of clinical outcomes. To further validate the effectiveness of immunotherapy, immune regulatory processes needed to be observable as well (IHC, Bulk RNA Sequencing). ELISA data showed notable changes in immune-dependent cytokine release by treatment type, and specific T-cell activation markers (CD25, CD69) were significantly upregulated in response to therapy.

Conclusion: This PMT model is one of the first to show a clinically relevant immunotherapy response by inducing tumor cell death. It also demonstrates therapy-dependent changes in T-cell activation, cytokine release and gene expression, highlighting immunotherapy's immunomodulatory impact on the tumor and its microenvironment.

O8

Therapeutic journey in a case of advanced urachal carcinoma: treatment approaches and clinical outcomes

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Background: Urachal cancer arises from remnant cells of the urachus, a fetal structure that connects the urinary bladder to the umbilical cord. It is a rare and aggressive adenocarcinoma, typically located at the dome of the bladder.

Case: A 46-year-old male patient presented with macrohematuria and underwent partial cystectomy, lymphadenectomy and appendectomy following the diagnosis of urachal carcinoma in July 2022. One year later, recurrent disease with retroperitoneal lymphadenopathy and pulmonary metastases was evident. The patient achieved macroscopic remission after five cycles of platin-based chemotherapy and 5-FU, followed by resection of residual lymph nodes. Three months later, disease progression with osseous and pulmonary manifestations necessitated further therapy. Radiation to the L2 vertebra and four cycles of docetaxel were administered. Unfortunately, he did not respond to this treatment and developed local recurrence in the bladder next to further pulmonal and retroperitoneal progress. Third-line therapy with FOLFIRI led to stable disease in the lungs after four cycles but further progression in the bladder and locoregional lymph nodes. Macrohematuria required palliative radiotherapy of the bladder and adjacent lymph nodes in November 2024.

Discussion: Urachal cancer is a rare and aggressive adenocarcinoma with limited therapeutic options in advanced disease. Based on retrospective analyses, chemotherapy with 5-FU and a platinum agent is the recommended first-line therapy. Our patient received three lines of systemic treatment combined with local therapy for metastatic disease and remains alive 17 months after the diagnosis of recurrent disease.

O9

NACT basierend auf ctDNA+ trotz primärer Resektabilität beim Pankreaskarzinom: 1-Jahres-Follow up von Patientin 0

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Einleitung: Präoperative detektierbare ctDNA (ctDNA+) stellt ein biologisches Hochrisiko auf Frührezidive für PankreaskarzinompatientInnen dar. Das mediane krankheitsfreie Überleben von ctDNA+ PatientInnen trotz kurativ intendierter primärer Resektion liegt in Beobachtungsstudien bei etwa 6 Monaten.

Der tatsächliche Überlebensvorteil durch Therapieänderung auf NACT statt Operation aufgrund von Liquid Biopsy Ergebnissen wurde bisher noch nie gezeigt.

Material und Methoden: Wir berichten den klinischen Ablauf und das 12-Monats-Follow Up der weltweit ersten Patientin nach Liquid Biopsy gesteuertem Therapieentscheid (NACT bei ctDNA+ trotz primärer Resektabilität und CA 19-9 < 500 U/ml) bei lokalisiertem Pankreaskarzinom.

Zeitpunkte für die Liquid Biopsy waren prätherapeutisch (t = 0), 3 Monate (t = 1), 6 Monate (t = 2 = Operation), 9 Monate (t = 3) und 12 Monate (t = 4) nach Therapiebeginn.

Ergebnisse: Die 70-jährige ECOG 0 Patientin wurde Anfang März 2024 bei primär resektablen Pankreaskopfkarzinom und CA 19-9 von 238,2 U/ml rekrutiert.

Die Liquid Biopsy war positiv auf KRAS G12/13 mit 8 positiven Tröpfchen (keine double positives) und einer MAF von 0,4 %. Das Screening dauerte 9 Tage.

Unter Studienbedingungen wurde eine neoadjvante Chemotherapie mit FOLFIRINOX (Dosisreduktion 1 ab I/15 wegen Diarrhö und Dosisreduktion 2 ab II/1 bei UGT1A1 mut.) eingeleitet. Nach 3 Zyklen wurde bei SOS-Syndrom abgebrochen und auf nab-Paclitaxel/Gemcitabine gewechselt.

Sowohl das 3-Monats-, als auch das 6-Monats-FUP zeigen bildgebend eine Stable Disease, weshalb die Exploration für Ende November 2024 (robotische Pankreatektomie) geplant wurde.

Am Kongress werden der molekularbiologische und klinische Verlauf inklusive 12-Monats-FUP präsentiert.

Schlussfolgerung: Ein Liquid Biopsy basierter Therapieswitch zusätzlich zum herkömmlich Goldstandard-Staging (anatomisch und CA 19-9) ist klinisch sicher und ohne Therapieverzug anwendbar.

O10

Personalized molecular diagnostics and therapies in patients with cancer – A single-center experience of an interdisciplinary Molecular Tumor Board platform

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Introduction: Interdisciplinary Molecular Tumor Boards (MTBs) are increasingly implemented to account for the growing complexity in molecular oncology and targeted cancer therapies. Here, we report updated results from patients admitted to the MTB Graz.

Methods: Personalized treatment recommendations are derived in a multi-step process, including individualized diagnostic procedures, pathologic classifications and clinical annotation of therapeutic options of detected alterations based on ESMO Scale of Clinical Actionability for molecular Targets (ESCAT) levels. Clinical and molecular-pathological data of patients referred to the MTB Graz are presented.

Results: Until October 1st 2024, 386 patients were admitted to the MTB Graz. The most frequent cancer types were pancreatic ($n=57$, 15%), colorectal ($n=44$, 11%), lung ($n=31$, 8%), breast ($n=26$, 7%), and biliary tract cancer ($n=20$, 5%). Molecular sequencing and/or immunohistochemistry evaluations were conducted in 365 patients (95%). In total, a personalized treatment recommendation was provided in 196 patients (54%), comprising ESCAT level I recommendations in 28%, level II in 24%, and level III in 48%. Preliminary treatment response data from 73 patients with MTB-recommended therapies and sufficient clinical follow-up were obtained, with a disease control rate of 45% and overall response rate of 29%. Exceptional treatment responses (i. e., ≥ 12 months duration of response) were observed in 12% of treated patients.

Conclusion: A targetable alteration was identified in the majority of patients with oftentimes advanced cancers admitted to the MTB. Promising treatment response patterns were observed in a subset of treated patients. Detailed molecular and clinical outcome data can be presented at the meeting.

O11

Adenokarzinom des ösophagogastralen Übergangs AEG Typ II nach Siewert: Haben wir endlich die optimale operative Strategie?

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Einleitung: Die Frage der optimalen OP-Methode für das Cardiakarzinom (AEG II) wird seit Jahrzehnten lebhaft diskutiert. Laut Guidelines kann beim AEG II eine Ösophagusresektion (IL) oder eine transhiatal erweiterte Gastrektomie (TEG) erfolgen. Inspiriert von asiatischen Berichten haben wir seit 2019 Erfahrung mit der proximalen Gastrektomie mit double tract Rekonstruktion (PG-DTR) gesammelt.

Methode: Wir präsentieren eine retrospektive Analyse perioperativer Daten und Überlebensdaten von PatientInnen, die von 2016 bis 2023 wegen eines potenziell kurativ resektablen AEG II operiert wurden. Die Ergebnisse von drei OP Methoden werden bezüglich onkologischer Qualitätskriterien, perioperativer Daten und des Überlebens verglichen.

Ergebnisse: Insgesamt wurden 92 Patienten (33 Frauen, 59 Männer) mit AEG II operiert, davon 32, 30 und 30 mittels IL, TEG bzw. PG-DTR mit einer R-0-Rate von 90%, 97% bzw. 94%. Die mediane Anzahl untersuchter Lymphknoten war 43, 33 bzw. 31, die mediane KH-Aufenthaltsdauer 11, 12 bzw. 12 Tage, die Rate schwerer perioperativer Komplikationen 12,5%, 26,7% bzw. 30% ($p=0.09$), die KH-Letalität 3,1%, 0% bzw. 0% (gesamt 1,1%). Anastomosenleaks wurden bei 3,3, 20 bzw. 9,4% beobachtet. Die kumulativen 1- und 3-Jahresüberlebensraten waren 93%, 89% bzw. 93 und 78%, 58% bzw. 82%.

Schlussfolgerung: Obwohl es sich bei der PG-DTR im Vergleich mit IL und TEG um einen limitierten Eingriff handelt, war der Erfüllungsgrad der onkochirurgischen Qualitätsparameter bei allen 3 OP-Methoden adäquat. Sowohl bzgl. perioperativer Sicherheit als auch bzgl. der Überlebensdaten erscheint die PG-DTR als gleichwertige Alternative. In unserer Erfahrung ist die Patienten-Akzeptanz gegenüber der PG-DTR spürbar höher als bei den Standardmethoden.

O12

Boosting immunotherapy in non-small cell lung cancer

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Background/Aims: Lung cancer remains the leading cause of cancer-related mortality worldwide. While immunotherapy has improved patient outcomes, achieving long-term remission remains a challenge. Inducing inflammatory cell death in tumor cells to alter the tumor immune microenvironment (TIM) may enhance immunotherapy responses. Plasma membrane rupture (PMR), a key event in lytic cell death, is associated with the release of damage-associated molecular patterns (DAMPs) that promote inflammation and shape the TIM. Recent studies identified Ninjurin 1 (NINJ1) as a critical mediator of PMR, with NINJ1 dysregulation observed in various cancers, though its specific role in lung cancer is not well understood. This study aims to characterize the role of NINJ1 in lung cancer and its potential as a therapeutic target.

Methods/Results: Using CRISPR/Cas9-mediated modulation of NINJ1 expression in lung cancer cell lines, we found that NINJ1 expression levels directly impact DAMP release from tumor cells. Bioinformatic analysis of publicly available datasets indicated that tumors with low NINJ1 expression exhibited reduced immune cell infiltration, correlating with shorter patient survival. For in vivo functional studies, we developed a unique murine lung cancer model allowing CRISPR-mediated targeting of NINJ1 specifically within tumor cells. Preliminary results suggest that NINJ1 has tumor-suppressive properties in lung cancer progression.

Conclusion: Our findings suggest that NINJ1 plays a critical role in modulating the TIM in lung cancer, with evidence supporting its function as a tumor suppressor. These results underscore the therapeutic potential of targeting NINJ1 and related regulators of lytic cell death to improve immune therapy in lung cancer patients.

O13

Ex vivo organ-perfusion of colorectal cancer liver metastasis (CRLM) – a novel cancer model

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Translation of cancer therapeutics into clinical use remains limited by the lack of reliable preclinical models that accurately represent the complex human tumor microenvironment (TME). Herein, we present the establishment and characterization of a novel ex vivo model for colorectal liver metastases (CRLM) using normothermic machine perfusion (NMP).

Whole human livers or resected liver specimens harboring CRLM ($n=7$) were subjected to NMP (OrganOx Metra) with a median perfusion time of 44.1(± 8.7) hours. Serial biopsies of metastases and liver-adjacent tissues were taken before and at the end of NMP. Single-cell RNA sequencing (scRNA-seq), spatial transcriptomics (ST), and multiplex immunofluorescence were used to assess tissue stability and structure during NMP.

Our multimodal approach generated for the first time a high-resolution scRNA-seq dataset of over 75,000 cells, encompassing expected cell types across tumor and liver tissues ($n=26$ samples). Initial model assessment confirmed metastatic CRC phenotypes by distinct iCMS classification. Further comparison of tissues revealed key features of its TME, including tumor associated SPP1+ macrophages and OLR1+ neutrophils. Importantly, analysis of compositional and transcriptomic stability of all respective cell populations confirmed minimal dynamic changes during NMP.

In summary, we provide the first time evidence that the NMP system can be used for establishing an ex vivo CRLM model characterized by only minimal changes of the cellular organ composition during the ex vivo period. We speculate that this model represents a novel cancer model to study CRLM biology in a near-physiological setting. The model may be used for preclinical drug testing in the future.

O14

Long term surveillance of medical and psychosocial late effects after cancer treatment in childhood and adolescence in IONA – Interdisciplinary Oncological Follow-up Clinic

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Introduction: Advanced medical care leads to high rates of cure up to 84% in patients with cancer in childhood and adolescence, but survivors have a high risk for disease and/or treatment related late toxicities. Physical conditions, cognitive function, mental health and psychosocial issues can be affected. During childhood short-term follow-up is performed in the children's hospitals. Afterwards patients often get lost to further surveillance due to lack of experience with treatment related late complications.

Methods: "IONA—Interdisciplinary Oncological Follow-Up Clinic" is offering age-appropriate medical and psychosocial long-term follow-up since 2020. This outpatient department was founded by cooperation between the City of Vienna and the Austrian Health Insurance Fund (ÖGK). The City of Vienna finances the major part of the project with support of the Children's Cancer Aid Wien-NÖ-BGLD. A team of one hemato/oncologist, two clinical psychologists, a social worker and two case managers provide individual medical care combined with psychosocial support.

Results: More than 600 survivors have been referred to IONA since 2020. The majority was diagnosed with CNS tumours, acute leukemia or lymphoma. Treatment related late toxicities affect every organ, most commonly bone metabolism, endocrine and cardiovascular system. Additionally neurocognitive impairment and mental stress have a negative impact on working life, quality of life and financial security.

Conclusion:

- IONA offers specialized long-term follow-up care for more than 600 survivors of cancer in childhood and adolescence.
- About 60 % of IONA patients show physical late effects in different organ systems.
- Mental stress and neurocognitive impairment require additional psychosocial support.

O15

Development and validation of a transcriptomic- and genetic-based model for predicting regorafenib response in metastatic colorectal cancer

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Introduction and Aims: Regorafenib (Rego), a multi-kinase inhibitor, is approved for refractory metastatic colorectal cancer (CRC) but shows efficacy only in a subset of patients, often associated with significant side effects. Identifying likely responders could optimize treatment outcomes and minimize toxicities.

Material and Methods: We developed a predictive model for Rego response using transcriptomic and genetic data from 41 CRC cell lines, classifying them based on drug sensitivity data from the CTRP2 database. RNA and DNA sequencing were used as predictors. Several machine learning algorithms (e.g. Random Forest, Generalized Linear Model via Elastic Net (GLMNET), Support Vector Machine) were applied, with GLMNET exhibiting the highest predictive performance. Model accuracy was evaluated using leave-one-out cross-validation. To validate the findings, the model was applied to transcriptomic data from >2000 CRC patients treated with Rego (Caris Life Sciences).

Results: GLMNET achieved superior predictive accuracy (AUC = 0.79) and outperformed other models in sensitivity, specificity, and calibration metrics. Key features included gene expression levels (e.g., FAM131A, SH3BP1, U2AF1) and mutations (e.g., RALGAPA1, MORC1). In external validation using the transcriptomic data of >2000 Rego-treated CRC patients, the model successfully identified responders, confirming its robustness. Gene-set and -pathway analyses revealed that responders had enrichment in cell-cycle regulation and DNA-

repair-pathways, while non-responders displayed characteristics of a stroma-rich microenvironment with endothelial and fibroblast infiltration.

Conclusion: Our GLMNET effectively predicts Rego response, validated in a large cohort of CRC patients. This predictive signature offers a promising tool for guiding personalized treatment strategies.

O16

Klinische Einordnung von Hodentumoren mittels multiparametrischer Magnetresonanztomographie (MRT) – Eine prospektive Single-Center Studie

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Einleitung und Fragestellung: Ziel dieser prospektiven Studie war es, den diagnostischen Wert der multiparametrischen Magnetresonanztomographie (MRT) bei der Unterscheidung maligner und benigner Hodentumoren zu evaluieren.

Material und Methoden: 48 männliche Patienten (medianes Alter 37,5 Jahre) mit sonographisch suspekten Hodenläsionen wurden mittels multiparametrischer MRT inklusive Diffusionsgewichteter Bildgebung (DWI) und dynamischer kontrastverstärkter MRT (DCE-MRT) untersucht. Alle Patienten erhielten eine histopathologische Untersuchung des Befundes durch Orchiektomie oder Hodenteilresektion. Für die statistische Auswertung wurden verschiedene Tests wie der Kolmogorov-Smirnov-Test, t-Test und logistische Regression angewendet.

Ergebnisse: Die mediane Tumorgröße betrug in der MRT 2,0 cm für maligne und 1,1 cm für benigne Tumoren ($p < 0{,}05$). Maligne Tumoren wiesen signifikante Unterschiede hinsichtlich des Enhancement-Musters ($p < 0{,}01$) und der Diffusionsrestriktion auf. Der minimale ADC-Wert betrug bei benignen Tumoren $0{,}9 \times 10^3$ mm²/s und bei malignen Tumoren $0{,}7 \times 10^3$ mm²/s ($p < 0{,}05$). Die multiparametrische MRT zeigte eine Sensitivität von 94,3%, eine Spezifität von 76,9%, einen positiven prädiktiven Wert von 91,7% und einen negativen prädiktiven Wert von 83,3%. Im Rahmen der Histologie zeigten sich 72,9% maligne und 27,1% benigne Tumore.

Schlussfolgerung: Die multiparametrische MRT bietet eine hohe diagnostische Genauigkeit zur Unterscheidung zwischen malignen und benignen Hodentumoren und stellt eine wertvolle Methode zur genauen Diagnose dar.

O17

Novum: Impact of the first liquid biopsy guided changes of treatment to NACT in ctDNA+ localized pancreatic cancer patients – an interim analysis

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Introduction: Preoperative detectable ctDNA (ctDNA+) represents a biological high-risk for early recurrence in pancreatic cancer patients (median DFS 6 months).

The actual survival benefit from therapy modification based on liquid biopsy (LB) data has never been demonstrated before.

Materials and Methods: We report the world's first clinical outcomes for patients following LB-driven therapy decisions (NACT for ctDNA+ vs. primary surgery for ctDNA-) in addition to common indicators (anatomically resectable, CA 19-9 < 500U/ml) for localized pancreatic cancer from an Austrian single-center analysis.

DNA analyses were performed using ddPCR on KRAS G12/13 and Q61 at 3 positive droplets.

The difference in clinical outcome based on LB-guided therapeutical change to NACT instead of upfront surgery will be presented at the conference.

Interim Results: To date, 23 primarily resectable pancreatic cancer patients were recruited from January to November 2024 in addition to 138 patients whose LB data was gathered observationally previously. The preoperative detection rate despite CA19-9 < 500 U/ml was 17.4%. Median screening duration was 9 days.

Early recurrence (DFS ≤ 6 months) was observed in 50% of ctDNA+ patients undergoing upfront surgery (previously ($n = 46$) 45.7%), but 0% of ctDNA+ patients undergoing therapeutical switch, matching the outcome of ctDNA- patients going for upfront surgery (0%, previously ($n = 89$) 11.2%).

Updated and extensive data will be presented at the congress.

Conclusion: Interim data shows that the method is safe, immediately clinically implementable, and is accompanied with a potential survival advantage.

Rollout to additional centers in Austria is currently prepared and final data is expected in 2026.

O18

Importance of MTB network for liquid biopsy-based testing and treatment recommendations in metastatic breast cancer in Austria

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Introduction and Aims: The Molecular Tumor Board (MTB) of the Center for Precision Oncology (Subzentrum Präzisionsonkologie) at the University Comprehensive Cancer Center Graz (UCCC Graz) facilitates availability of valid testing methods and interdisciplinary interpretation. Circulating tumor DNA (ctDNA) enables repeated testing to evaluate tumor heterogeneity and resistance-related alterations. The approval of the selective estrogen receptor degrader (SERD) Elacestrant for treatment of hormone receptor positive, metastatic breast cancer (HR+ mBC) with ESR1 mutations highlighted the need for structured testing and interpretation, even in early treatment lines. A pilot project was launched in November 2023.

Material and Methods: Each institution in Austria was able to participate. Tumor fraction was estimated from shallow whole genome sequencing (WGS) using the ichorCNA algorithm. The AVENIO ctDNA Expanded Kit, a comprehensive genomic profiling (CGP) assay, was used to assess variants in 77 genes. The results of analyses were discussed interdisciplinary and clinically annotated at the MTB.

Results: Of 150 planned, to date 136 samples have been analyzed. As of August 2024, 123 samples of 115 patients were annotated in MTB. In 26 patients (22.6%) an ESR1 mutation was detected, 17 (14.8%) had ESR1 mutations below the limit of detection of a variant allele frequency (VAF) < 0.5%. PIK3CA mutations were detected in 35 patients (30.4%), BRCA 1/BRCA 2 mutations were detected in 6 (5.2%).

Conclusion: The ESR1 project demonstrated a feasible strategy to implement precision medicine based on ctDNA in clinical routine. The context of MTB enables a structured assessment of clinical relevance of detected mutations.

O19

Gemcitabine maintenance after first-line treatment with gemcitabine plus nab-paclitaxel in patients with locally advanced or metastatic pancreatic cancer: a retrospective single-centre analysis

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Introduction: The combination of gemcitabine/nab-paclitaxel is a common regimen for advanced pancreatic cancer (PDAC). Cumulative toxicity, particularly neuropathy is a significant concern associated with nab-paclitaxel, prompting gemcitabine monotherapy as a maintenance strategy, given its efficacy in PDAC. However, limited data exists on this approach.

Methods: This retrospective analysis included patients treated at our institution from September 2016 to November 2022 with histologically or cytologically confirmed locally advanced or metastatic PDAC, who achieved disease control after first-line gemcitabine/nab-paclitaxel and transitioned to gemcitabine monotherapy for maintenance. Gemcitabine monotherapy was given at 2200 mg/m^2 on days 1 and 15 of a 28-day cycle. Kaplan-Meier estimates were used to assess overall survival (OS) and progression-free survival (PFS).

Results: We identified 16 patients achieving either stable disease ($n=6$) or partial response ($n=10$) after treatment with gemcitabine/nab-paclitaxel and then transitioned to gemcitabine maintenance therapy. Gemcitabine/nab-paclitaxel was discontinued after a median of 6 cycles. Maintenance with gemcitabine was stopped after a median of 3 cycles. Radiological assessment was feasible in 13 patients, with disease control maintained in 4 patients (31%) during gemcitabine maintenance. The remaining patients progressed. Median PFS was 9.8 months, with a median PFS on maintenance (PFS-2) of 2.7 months and a median OS of 14.1 months.

Conclusion: Gemcitabine maintenance therapy showed limited efficacy, though a subset of patients appeared to benefit. The results are limited by the small sample size and its ret-

rospective nature. Therefore, larger, prospective studies are needed to further evaluate the role of maintenance therapy in pancreatic cancer.

O20

Pathogenic ESR1 mutations in patients with HR+, HER2- metastatic breast cancer

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Introduction and aims: Elacestrant is the first selective estrogen recepetor degrador (SERD) approved for treatment of metastatic hormone receptor positive HER2 negative breast cancer (HR+, HER2- mBC) harboring an ESR1 mutation. Circulating tumor DNA (ctDNA) in plasma enables a non-invasive method for mutation testing, especially for developing ESR1 mutations. To facilitate the access to ctDNA testing for ESR1 mutations in HR+ HER2- mBC a project in the framework of the Molecular Tumor Board (MTB) including the analysis 150 plasma samples was launched in November 2023.

Material and methods: To screen for ESR1-mutations, the AVENIO ctDNA Expanded Kit, a hybrid capture based platform to enrich for 77 clinically relevant genes was used. Prevalence of ESR1 mutations across the cohort was calculated.

Results: Of 150 planned samples, 136 cases have been collected to date. As of August 2024, 123 plasma samples from 115 patients have been analyzed, including 8 patients who underwent blood draws at multiple time points. 26 patients (22.6%) had an ESR1 mutation, 17 (14.8%) had an ESR1 mutation below the detection limit at a variant allele frequency (VAF) of 0.5%. The most common ESR1 mutations were D538G (35.8%), Y537S (25.7%), E380Q (10.4%) and Y537N (10.4%). The proportion of detected ESR1 mutations increased with treatment lines with 32% after 1st line, 37% after 2nd line and 47% after 3rd line treatment.

Conclusion: ESR1 mutations in this heterogenous cohort were detected in 22.6% of patients. The most common ESR1 mutations were D538G, Y537S, E380Q and Y537N comparable to previously reported trials.

Palliativmedizin

P1

Wissen österreichischer Ärzt*innen zu Palliativversorgung, assistiertem Suizid und palliativer Sedierung: Eine explorative Studie

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Hintergrund: Seit Januar 2022 ist assistierter Suizid (AS) in Österreich legal, sofern bestimmte Bedingungen erfüllt sind. Das kürzlich eingeführte Bundesgesetz zur Sterbehilfe erlaubt medizinischen AS für schwerkranke Personen mit unheilbaren, lebensbeendenden Erkrankungen oder für Menschen mit schweren, andauernden Krankheiten, die ihr Leben erheblich beeinträchtigen. Palliative Sedierungstherapie (PST) beschreibt den kontrollierten Einsatz von Medikamenten, um einen Zustand reduzierten oder fehlenden Bewusstseins (Bewusstlosigkeit) herbeizuführen und so ansonsten unbehandelbares Leiden zu lindern. Ziel dieser Studie war es, das Wissen österreichischer Ärztinnen und Ärzte zu AS und PST zu bewerten und die Wissensstände zwischen Palliativmedizinerinnen (PC) und Nicht-Palliativmedizinerinnen zu vergleichen.

Methoden: In dieser explorativen Studie wurde eine Online-Befragung unter Ärztinnen und Ärzten in Österreich durchgeführt. Die Fragen der Umfrage konzentrierten sich auf grundlegendes Wissen zu den Prinzipien der Palliativversorgung (PC),

des AS und der PST. Zu den Teilnehmer*innen zählten Ärztinnen und Ärzte mit Fachkenntnissen in PC sowie Ärztinnen und Ärzte anderer medizinischer Fachrichtungen.

Ergebnisse: 223 Ärztinnen und Ärzte schlossen die Umfrage ab. PC-Ärztinnen wiesen signifikant häufiger eine spezialisierte Ausbildung auf, wobei 74,2% ein PC-Diplom besaßen, verglichen mit 17,9% der Nicht-PC-Ärztinnen ($p<0{,}001$). In der klinischen Praxis identifizierten PC-Ärztinnen lebenslimitierende Erkrankungen wie COPD (93,3% vs. 79,9%, $p=0{,}007$), Herzinsuffizienz (91% vs. 76,9%, $p=0{,}007$) und Lebererkrankungen (80,9% vs. 68,7%, $p=0{,}0453$) präziser. Hinsichtlich der PST hielten sich PC-Ärztinnen häufiger an Leitlinien und verwendeten Midazolam (97,8% vs. 77,6%, $p<0{,}001$), Propofol (56,2% vs. 38,1%, $p=0{,}009$) und Levomepromazin (23,6% vs. 11,2%, $p=0{,}016$). Im Bereich AS legten PC-Ärztinnen häufiger Wert auf die Entscheidungsfähigkeit der Patientinnen ($p=0{,}006$) und waren besser über gesetzliche Anforderungen informiert. Beide Gruppen erkannten die Bedeutung von PC-Beratungen, wobei PC-Ärzt*innen häufiger der Meinung waren, dass diese AS verhindern können (47,2% vs. 23,9%, $p=0{,}001$).

Schlussfolgerung: Insgesamt zeigen österreichische Ärztinnen und Ärzte unzureichende Kenntnisse zu AS und PST, was den Bedarf an verstärkter Aufklärung zu den Prinzipien der Palliativversorgung unterstreicht, um eine informierte Praxis nach der Legalisierung von AS zu gewährleisten. Dennoch zeigen PC-Ärztinnen in Österreich eine überlegene Einhaltung von Leitlinien im Umgang mit lebenslimitierenden Erkrankungen, PST und AS im Vergleich zu Nicht-PC-Ärztinnen, was die Bedeutung einer spezialisierten Palliativausbildung hervorhebt.

P2

Palliative Strahlentherapie am Lebensende: Eine retrospektive Analyse der Einflussfaktoren auf die Anwendung der Strahlentherapie bei fortgeschrittener Tumorerkrankung

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Hintergrund: Palliative Strahlentherapie (RT) am Lebensende (EOL) bei fortgeschrittener Tumorerkrankung ist umstritten. Obwohl die EOL RT tumorbedingte Symptome lindern kann, tritt die Linderung in der Regel erst Wochen bis Monate nach der Behandlung ein, sodass die EOL RT potenziell die Lebensqualität der Patient:innen in der letzten Lebensphase beeinträchtigen kann. Ziel dieser Studie war es, potenzielle Faktoren zu bewerten, die den Entscheidungsprozess hinsichtlich einer RT am EOL beeinflussen könnten.

Methoden: In diese retrospektive Studie wurden 684 konsekutive Patient:innen mit der Diagnose eines soliden Tumors eingeschlossen, die zwischen 2017 und 2021 verstarben. Diese Patient:innen wurden in Bezug auf die EOL RT analysiert.

Ergebnisse: Insgesamt wurden 684 Patient:innen untersucht. Eine palliative RT wurde bei 164 Patient:innen durchgeführt, von denen 60 (36,6%) in den letzten 30 Lebenstagen eine EOL RT erhielten, wie in dieser Studie definiert. Die mediane Zeitspanne von der letzten palliativen RT bis zum Tod betrug bei allen Patient:innen, die eine RT erhielten, 55 Tage. Faktoren mit signifikantem Einfluss auf die Durchführung einer EOL RT waren: Alter ≤65 Jahre (OR 1,75, 95% KI 1,02–3,01), UICC-Stadium IV (OR 2,77, 95% KI 1,41–5,46), Lungenkrebs (OR 2,16, 95% KI 1,00–4,68), Überweisung an die Palliativversorgung (OR 1,80, 95% KI 0,98–3,30), systemische Tumortherapie ≤30 Tage vor dem Tod (OR 1,87, 95% KI 1,05–3,33), ECOG-Performance-Status ≥2 (OR 3,73, 95% KI 1,88–7,40), Bestrahlung mehrerer Körperstellen (OR 2,08, 95% KI 1,00–4,29) und ≤5 angewandte Fraktionen (OR 2,37, 95% KI 1,23–4,57).

Schlussfolgerung: Diese Ergebnisse unterstreichen die unterschiedlichen Muster der RT in Abhängigkeit von bestimmten Faktoren, die die Durchführung einer EOL RT beeinflussen, und zeigen die Komplexität der Behandlungsentscheidungen bei fortgeschrittenen Tumorerkrankungen auf. Wesentliche Faktoren für personalisierte, patientenzentrierte Behandlungsentscheidungen am EOL, wie die RT, konnten identifiziert werden und sollten weiter untersucht werden.

P3

Erkennung von Palliative-Care-Bedürfnissen in der Inneren Medizin: Retrospektive Analyse mit dem *P*-CaRES-Tool

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Hintergrund: An internistischen Abteilungen gibt es häufig Patient:innen mit lebenslimitierenden Erkrankungen und nicht

erfüllten Palliative-Care-(PC)-Bedürfnissen. Ein Großteil der Patient:innen, die von PC profitieren könnten, wird nicht identifiziert, wodurch ihre PC-Bedürfnisse unbeachtet bleiben. Das Screening-Instrument Palliative Care and Rapid Emergency Screening (*P*-CaRES) wurde bereits validiert, um Patient:innen mit PC-Bedürfnissen in der Notfallversorgung zu identifizieren. Um zu überprüfen, ob die nicht erfüllten PC-Bedürfnisse von Patient:innen, die in Abteilungen der Inneren Medizin aufgenommen werden, mithilfe des *P*-CaRES-Instruments erkannt werden können, wurde dieses Instrument in einer Patient:innengruppe in Abteilungen der Inneren Medizin getestet.

Material und Methoden: Zur Ermittlung des Anteils an Patient:innen mit PC-Bedürfnissen in der Inneren Medizin wurden retrospektiv alle Patient:innen gescreent, die in einem der beiden Bereiche der Inneren Medizin unseres Krankenhauses aufgenommen wurden. Dabei wurden zwei Zeiträume abgedeckt: 01.10.2019–31.12.2019 und 01.03.2020–31.05.2020, wobei der zweite Zeitraum mit dem Beginn der SARS-CoV-2-Pandemie zusammenfiel. Im ersten Schritt des Screening-Instruments wurden Patient:innen mit mindestens einer lebenslimitierenden Erkrankung (life-limiting disease, LLD) für eine weitere Analyse ausgewählt. Im zweiten Schritt wurde überprüft, ob diese Patient:innen mindestens zwei PC-Bedürfnisse hatten. Das postulierte Bedürfnis wurde mit der tatsächlichen Versorgung der Patient:innen verglichen, insbesondere ob PC-Konsultationen durchgeführt wurden.

Ergebnisse: Insgesamt wurden 2509 Patient:innen im Hinblick auf LLD und PC-Bedürfnisse in den beiden Zeiträumen gescreent. Das *P*-CaRES-Instrument identifizierte 631 Patient:innen mit mindestens einer LLD, von denen 452 (71,63%) PC-Bedürfnisse aufwiesen. Insgesamt wurden 132 (20,92%) Patient:innen an ein PC-Team überwiesen. Patient:innen mit LLD und PC-Bedürfnissen hatten eine signifikant kürzere Überlebenszeit im Vergleich zu Patient:innen mit nur einer LLD.

Schlussfolgerungen: Die Anzahl der Patient:innen mit nicht erfüllten PC-Bedürfnissen in Abteilungen der Inneren Medizin ist sehr hoch. Dennoch sind Konsultationen von PC-Teams selten. Das *P*-CaRES-Instrument konnte Patient:innen mit PC-Bedürfnissen in Abteilungen der Inneren Medizin identifizieren und zeigt damit sein Potenzial für den Einsatz sowohl in der Notfall- als auch in der Inneren Medizin. Darüber hinaus konnte das *P*-CaRES-Instrument das Überleben vorhersagen.

P4

Hypnose als Intervention für das Legen eines Peripher Inserierten Zentralvenösen (PICC)-Katheters bei Patient:innen im Rahmen eines palliativen Settings

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Einleitung und Fragestellung: In der palliativen Versorgung stellt die Platzierung eines PICC-Katheters (peripher eingeführter zentraler Venenkatheter) eine häufige Intervention dar. Ziel dieser Pilotstudie ist es, den Einsatz hypnotischer Interventionen in das Punktionsmanagement bei der PICC-Katheterplatzierung zu integrieren, um den Eingriff für Patient:innen sowie Punkteur:innen zu erleichtern. Die Untersuchung fokussiert auf die Reduktion von Schmerz, Angst und Stressreaktionen sowie die Verminderung des Medikationsbedarfs.

Material und Methoden: Die Pilotstudie umfasst eine Interventionsgruppe ($n=5$), bei der eine Kombination aus Lokalanästhetikum und Hypnose angewendet wird sowie eine Kontrollgruppe ($n=5$), die nur mit Lokalanästhetikum behandelt wird. Die Hypnosetechniken umfassen Induktion, Vertiefung, Dehypnose und posthypnotische Suggestionen. Prä- und postinterventionelle Zielparameter wie Schmerzintensität (VAS), Angst (STAI), Entspannung (NRS) und emotionale Befindlichkeit (EWS) werden erfasst und ausgewertet. Die Auswertung erfolgt mittels t-Tests und visueller Darstellung der Ergebnisse in Säulendiagrammen, die die Veränderung der Schmerzintensität und anderer Parameter dokumentieren.

Ergebnisse: Die Datenerhebung findet derzeit im stationären palliativen Setting statt. Vorläufige Daten deuten auf einen positiven Effekt von Hypnose auf Schmerz, Angst und postinterventionelle Erholung hin.

Schlussfolgerungen: Die Integration von Hypnose in das Punktionsmanagement bei der Anlage von PICC-Kathetern in der Palliativmedizin könnte zu einer signifikanten Entlastung, einer Reduktion der Medikation und einer höheren Zufriedenheit führen.

P5

Existenzielles Leid – Die untrennbare Voraussetzung für Sterbewünsche

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Einleitung: Sterbewünsche werden bei 1–44% der Patient:innen in Palliativsituationen beobachtet. Sterbewunsch und Lebenswille bestehen oft gleichzeitig, wobei deren Intensität fluktuieren kann. Definiert werden Sterbewünsche als eine Reaktion auf Leiden im Zusammenhang mit einem lebensbedrohlichen Zustand, in dem Patient:innen keinen anderen Ausweg sehen, als das Sterben zu beschleunigen. Sie wollen "so" nicht leben.

Fragestellung: Was sind die Hintergründe, die zur Entwicklung von Sterbewünschen führen?

Material und Methoden: Ein narratives Review englischer und deutscher Publikationen in PubMed unter Verwendung von Schlüsselbegriffen im Zusammenhang mit existenziellem Leid (EL) und Sterbewünschen, von 1950 bis Oktober 2024; zusätzlich selektive Suche in der Fachliteratur zur Existenzanalyse.

Ergebnisse: Die Existenzanalyse bietet die kohärentesten Erklärungen für die dem EL zugrundeliegenden Prozesse. EL betrifft 24–35% der Patient:innen in Palliativsituationen und ist eine bedrohliche multidimensionale Erfahrung, wenn die gewohnten Voraussetzungen für ein gutes Leben verloren gehen, beispielsweise durch Gefühle wie Ohnmacht, Kontrollverlust, Rollenverlust, in der Erkrankung gefangen sein oder anderen zur Last fallen. Im Falle eines anhaltenden, allumfassenden Gefühls der Sinnlosigkeit und Hoffnungslosigkeit entwickelt sich Verzweiflung. Frankl spricht von "existenziellem Vakuum", aus dem sich Sterbewünsche entwickeln.

Die einzige wirksame Unterstützung sind Gespräche mit reflektierenden Zuhörenden, um die Patient:innen zu befähigen, ihre persönliche Einstellung an ihre Situation anzupassen. Medikamente sind wirkungslos.

Schlussfolgerung: Sterbewünsche sind ein komplexes Phänomen und untrennbar mit der Erfahrung des existenziellen Leids verbunden. EL ist eine multidimensionale Erfahrung, die aufgrund von empfundener Hoffnungslosigkeit und Sinnlosigkeit zu Verzweiflung und schließlich zum Sterbewunsch führen kann. Begleitet durch kompetente Betreuungspersonen können existenziell leidende Patient:innen eine geänderte Einstellung und wieder Lebensqualität finden.

P6

Assistierter Suizid – Auswirkungen des Sterbeverfügungsgesetzes auf Fachkräfte in Palliative Care

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Einleitung und Fragestellung: Mit dem Inkrafttreten des Sterbeverfügungsgesetzes am 1. Januar 2022 wurde der assistierte Suizid (AS) in Österreich legalisiert. Diese gesetzliche Neuerung stellt Fachkräfte in der Palliativversorgung vor erhebliche ethische, emotionale und praktische Herausforderungen. Diese Entwicklung hinterfragt die Grundprinzipien von Palliative Care, die darauf abzielen, Leiden zu lindern und die Lebensqualität zu verbessern, ohne aktiv in den Sterbeprozess einzugreifen. Diese Studie untersucht die Auswirkungen des Gesetzes auf den Arbeitsalltag von Fachkräften in der Palliative Care.

Material und Methoden: Qualitative, problemzentrierte Interviews mit 14 Fachkräften unterschiedlicher Professionen aus mobilen und stationären Palliativeinrichtungen wurden durchgeführt. Die Daten wurden mittels reflexiver thematischer Analyse analysiert, um Erfahrungen, Herausforderungen und Unterstützungsbedarf der Fachkräfte zu erfassen.

Ergebnisse: Die Entwicklung von Akzeptanz der Betreuenden gegenüber der Entscheidung der Patient*innen für AS ist ein bemerkenswertes Ergebnis dieser Studie. Akzeptanz zeigt sich als multidimensionaler Prozess, entscheidend geprägt durch Reflexion und einen relationalen Zugang. Dieser berücksichtigt die individuellen Bedürfnisse, Werte und Umstände der Patient*innen und ermöglicht eine differenzierte Beurteilung jeder einzelnen Situation. Unterstützende Strukturen wie klare Richtlinien und offene Kommunikationsräume fördern diesen Prozess.

Schlussfolgerung: Durch die Auseinandersetzung mit dem Sterbeverfügungsgesetz wurde ein Reflexions- und Anpassungsprozess angestoßen, der zu mehr Respekt und Akzeptanz gegenüber den Entscheidungen von Patient*innen für AS geführt hat. Diese Akzeptanz unterstützt Fachkräfte dabei, Patient*innen professionell zu betreuen, auch wenn die Entscheidungen der Patient*innen nicht mit der persönlichen Einstellung übereinstimmen, ohne dabei die eigene Integrität zu verletzen. Institutionelle Unterstützung durch klare Leitlinien, kontinuierliche Weiterbildung und interprofessionellen Austausch sind entscheidende Faktoren in diesem Prozess.

P7

Vermeide! Verwende? Beende? – Das arzneimittelinduzierte Delirrisiko bei Palliativpatient:innen

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Patient:innen mit fortgeschrittener Grunderkrankung haben u. a. aufgrund von metabolischen Veränderungen und der Anwendung von Arzneistoffen mit delirogenem Potential ein deutlich erhöhtes Risiko ein Delir zu entwickeln. Mit Fortschreiten der Erkrankung und der Aufnahme auf die Palliativstation nimmt die Zahl delirogener Medikamente zur Symptomkontrolle unweigerlich zu. Daher stellt sich die Frage: Kann das arzneimittelinduzierte Delirrisiko durch eine möglichst frühzeitige Medikationsanalyse und Anpassung der Medikamente gesenkt werden?

Für die vorliegende Querschnittstudie wurden drei Bewertungsskalen zur Einschätzung des arzneimittelassoziierten Delirrisikos ausgewählt und kombiniert. Über einen Beobachtungszeitraum von drei Monaten wurden retrospektiv anhand der Fieberkurven von 89 Patient:innen jene Arzneistoffe identifiziert, die (i) bei Erstvorstellung auf der Palliativstation des Kepler Universitätsklinikums häufig verordnet und (ii) durch ein delirogenes Potential gekennzeichnet sind. Beide Kriterien wurden mittels Eisenhower-Matrix quantitativ ausgewertet und priorisiert.

Es wurde festgestellt, dass einerseits die Medikamentenlast bei dieser Personengruppe sehr hoch ist (Ø15,6 Arzneistoffe/Patient:in), andererseits das delirogene Potential bei fast einem Viertel der verordneten Arzneistoffe als hoch (4,57%) oder moderat (19,81%) einzustufen ist. 82% der untersuchten Patient:innen waren von einem erhöhten medikamenteninduzierten Delirrisko bedroht. Für die 15 am höchsten priorisierten Arzneistoffe wurden konkrete Handlungsempfehlungen hinsichtlich eines möglichen Absetzens oder einer Umstellung auf nicht oder weniger delirogene Wirkstoffe ausgearbeitet. Eine exemplarische Anpassung der untersuchten Medikationslisten senkte den Anteil der Patient:innen “at risk” um 17,9%.

Es konnte gezeigt werden, dass das hohe arzneimittelbezogene Delirrisiko bei Patient:innen in Erstvorstellung auf der Palliativstation durch strukturierte Maßnahmen gesenkt werden kann. Untersuchungen im klinischen Setting bzgl. der potenziellen Verringerung der Delirhäufigkeit wären als nächster Schritt sinnvoll.

P8

„Ich hab es im Gefühl“ – Early Integration von Palliative Care bei onkologischen Patient*innen durch Verwendung von Assessmentinstrumenten

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Hintergrund: Krebserkrankungen sind immer noch für ein Viertel der jährlichen Todesfälle verantwortlich. Die S3-Leitlinie Palliativmedizin nennt als Zeitpunkt für die Integration von Palliative Care die Diagnosestellung einer nicht heilbaren Krebserkrankung unabhängig davon ob noch tumorspezifische Therapien vorgesehen sind oder nicht. Die vorliegende Arbeit entstand durch das Interesse an der Einleitung palliativer Versorgung onkologisch erkrankter Menschen im Krankenhaus. Von zentralem Interesse war es zu untersuchen, wie die Identifikation von Menschen mit Palliativversorgungsbedarf von statten geht.

Forschungsfragen: Welche Relevanz hat die Verwendung der, von der S3-Leitlinie Palliativmedizin empfohlenen, Assessmentinstrumenten auf die frühzeitige Integration von Palliative Care bei onkologischen Patient*innen im Krankenhaus?

Welche Maßnahmen/Handlungen können zusätzlich Auswirkung auf die frühzeitige Einbeziehung von Palliative Care in das Behandlungskonzept haben?

Ziel: Diese Arbeit soll die derzeitige Verwendung von Assessmentinstrumenten, zur Identifikation von onkologischen Patient*innen mit Palliativversorgungsbedarf, in Krankenhäusern darstellen und zugleich den möglichen Benefit dieser zeigen.

Methodik: Es erfolgte eine Literaturrecherche um daraus den Theorieteil zu verfassen. Ein quantitatives, deskriptives Forschungsdesign wurde angewandt. Die Forschungsfragen wurden explorativ ausgewertet.

Ergebnisse: Es konnte kein Hinweis darauf gefunden werden, dass die Verwendung der empfohlenen Assessmentinstrumenten zu frühzeitiger Integration von Palliative Care führt, da diese zu wenig bekannt sind, um genutzt zu werden. Auch andere Faktoren zugunsten der Early Integration von Palliative Care konnten nicht identifiziert werden.

Schlussfolgerung: Wie schon in der Literatur beschrieben, dürfte es sich um einen multifaktoriellen Prozess handeln. Der Einsatz von strukturierten Screenings um Patient*innen mit hoher Symptomlast identifizieren zu können ist dennoch empfohlen und dient der Sicherstellung der Qualität der Betreuung von schwerkranken Menschen.

Klinische Studie

S1

AGMT_aMYELOIDr: Austrian Myeloid Registry

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The Austrian Myeloid Registry (AMR) is a non-interventional study. It collects data from patients with the myeloid diseases like myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML), acute myeloid leukemia (AML), primary myelofibrosis (PMF), chronic myeloid leukemia (CML), and other rarer disease subtypes. The AMR is multi-center database and collects data at various sites in Austria and potentially also at other centers in other countries in future. The registry has an electronic case report form (eCRF), where all data is entered by clinical trial personnel and/or physicians. The registry also consists of patients previously documented in the Austrian Registry of Hypomethylating Agents.

The registry is intended as a long-term project. The initial medium-term goal regarding patient numbers will be 3000 (incl. patients of HMA Registry) documented patients.

The goal of the Austrian Myeloid Registry is to build a disease-specific registry aimed at assessing the therapeutic landscape of patients with myeloid diseases. Our intention is to advance our knowledge on the natural course of these diseases in untreated or best supportive care (BSC) treated patients, as well as the efficacy and toxicity and sequence of use of various treatments in a routine clinical setting.

Primary objective: To assess the treatment patterns (therapeutic landscape) of patients with myeloid diseases.

S2

AGMT Austrian CLL (chronic lymphocytic leukemia) Registry

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This registry is designed as multicenter observational cohort of patients with CLL.

The goal of this registry is to build a disease-specific registry aimed at assessing the therapeutic landscape of patients with CLL in Austria. It will be set up to collect real-world experience in the management of patients with this disease. This registry will collect data at various sites in Austria. The aim is to gain valuable insights on both efficacy and toxicity, as well as the sequence of use of various treatments in a routine clinical setting.

Primary objective:

- To describe general characteristics of CLL patients
- To describe genetic risk profiles
- To describe the proportion of CLL patients in Austria that require treatment
- To describe concomitant diseases at diagnosis of CLL
- To describe treatment and outcome of treatment

- To describe patient outcome (e. g. in patients with chemoimmunotherapy and patients with targeted therapy)
- To describe toxicity with a focus on infections, cardiotoxicity, nephrotoxicity bleeding, etc.

Recruitment: About 500 patients will be included in this registry. This number may be revised over time as interest and demand dictates.

S3

AGMT Lung Cancer Registry

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This registry is designed as multicenter observational cohort of patients with lung cancer.

It will be set up to collect real-world experience in the management of patients with this disease. This registry will collect data at various sites in Austria. The aim is to gain valuable insights on both efficacy and toxicity, as well as the sequence of use of various treatments in a routine clinical setting.

Indication: The registry will be made available for all disciplines and physicians caring for cancer patients and will include patients ≥ 18 years with locally advanced or metastatic lung cancer (advanced or metastatic stage patients in Austria (Stage III A-C and IV A-B NSCLC, limited disease (LD) and extensive disease (ED) SCLC)).

Primary objective:

- To describe the general characteristics of advanced or metastatic stage patients in Austria and molecular testing in patients with advanced or metastatic lung cancer
- To describe and characterize subgroups
- To describe treatment and outcome of treatment
- To describe patient outcome by means of overall survival and progression free survival
- To describe toxicity with a focus on immune related adverse events

Recruitment: 500 patients (this number may be revised over time as interest and demand dictates).

S4

AGMT_MBC-Registry – Metastatic breast cancer in Austria

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This registry is a prospective and retrospective, multicenter collection of data on patients with metastatic breast cancer in Austria. All tumor characteristics, medical histories and also treatment sequences are documented in anonymized form. For documentation in the registry, no further diagnostic or therapeutic measures are required than those already necessary in general. Participation in the registry must not interfere with treatment routines. A written consent must be obtained prior to the input of data. No informed consent is required from deceased patients.

Indication:

- Histological evidence of breast cancer
- Histological and/or radiological evidence of metastases
- Metastasis within 10 years of registry initiation

Primary objective: Epidemiological evaluations (general characteristics of metastatic stage patients in Austria, assessment of metastatic stage breast cancer subtypes in Austria, assessment of the specific characteristics and frequency of metastatic breast cancer, data on survival of female patients with metastatic breast cancer in Austria) and therapy-specific evaluations.

Recruitment: 2000–3000 patients.

S5

GMMG-HD8/DSMM XIX: A randomized phase-III non-inferiority trial assessing lenalidomide, bortezomib, dexamethasone induction-therapy with intravenous or subcutaneous isatuximab in transplant-eligible patients with newly diagnosed multiple myeloma

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This is a prospective, multicenter, randomized, parallel group, open-label, phase III clinical trial. After completion of the screening phase patients will be randomly assigned in a 1:1 ratio stratified by R-ISS stages I/II versus III versus not classified, and body weight.

End of the interventional treatment will be at the end of induction therapy including mandatory response assessment and bone marrow aspirate for all participants. End of study is planned after first HDM/ASCT and includes mandatory response assessment and BMA for all participants.

Primary objective: Demonstration of non-inferiority of subcutaneous (SC) isatuximab compared to intravenous (IV) isatuximab, both in combination with RVd, with respect to rates of VGPR or better after induction therapy.

Population: Adult female or male patients up to the age of 70 years inclusive with previously untreated MM requiring systemic treatment.

S6

GMMG-HD9/DSMM XVIII: A randomized phase-III trial assessing iberdomide versus iberdomide plus isatuximab maintenance-therapy post-autologous hematopoietic stem-cell-transplantation in patients with newly diagnosed multiple myeloma

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The GMMG-HD9/DSMM XVIII will be the maintenance trial subsequent to the GMMG-HD8/DSMM XIX trial covering first-line treatment for transplant-eligible patients with newly-diagnosed multiple myeloma within Germany and Austria. The trial is a prospective, multicentre, randomised, parallel group, open-label, phase III clinical trial. After completion of the screening phase, patients will be randomly assigned in a 1:1 ratio to either arm A (iberdomide) or arm B (iberdomide + isatuximab). Patients will be stratified by minimal residual disease negativity in the bone marrow and single vs. tandem HDM/ASCT. Throughout the study period yearly bone marrow assessments will be performed. End of the interventional treatment will be after 36 months of maintenance therapy (± 8 weeks) including mandatory response assessment and BMA for all participants.

End of the interventional treatment will be at the end of induction therapy including mandatory response assessment and bone marrow aspirate for all participants. End of study is planned after first HDM/ASCT and includes mandatory response assessment and BMA for all participants.

Primary objective: Demonstration of superiority of iberdomide plus isatuximab compared to iberdomide with respect to bone marrow minimal residual disease (MRD) negativity rates after two years of maintenance therapy.

Key secondary objective: Demonstration of superiority of iberdomide plus isatuximab compared to iberdomide with respect to progression-free survival (PFS).

S7

ARIADNE: Zanubrutinib (Brukinsa®) in patients with Waldenström's Macroglobulinemia (WM), Chronic Lymphocytic Leukemia (CLL), Marginal Zone Lymphoma (MZL) and Follicular Lymphoma (FL) – A prospective multicenter observational cohort study

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A non-interventional, open-label, prospective, single arm, multicenter, international multicohort study in Germany and Austria. The implementation of this non-interventional study (NIS) does not influence the physician's decision regarding therapeutic strategy, diagnostic methods, frequency of medical examinations and other procedures during and after the treatment. All data will be obtained in routine clinical practice.

Population: Adult patients (≥ 18 years) with Waldenström's macroglobulinemia (WM) Chronic lymphocytic leukemia (CLL), Marginal zone lymphoma (MZL) and Follicular lymphoma (FL) in need of treatment with decision for treatment with zanubrutinib (Brukinsa®) according to the Summary of Product Characteristics (SmPC).

Objective: The objective of this NIS is to evaluate medical resource utilization, where data is rare in all cohorts, patient's QoL and effectiveness of zanubrutinib treatment in adult patients with WM, CLL, MZL and FL in a real-world setting.

S8

R-Pola-Glo: Rituximab in combination with glofitamab and polatuzumab vedotin in patients with previously untreated aggressive B-cell lymphoma ineligible for R-CHOP

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Design: Prospective, open label, multicenter, bi-national (Germany and Austria) one arm phase-II-study with Rituximab (R) in combination with polatuzumab vedotin (Pola) and glofitamab (Glo) in patients with previously untreated DLBCL ineligible for R-CHOP chemotherapy (R-Pola-Glo).

Population: Previously not treated patients diagnosed with a histologically confirmed aggressive large B-cell lymphoma above >60 years of age not eligible for a fully dosed R-CHOP-like therapies will be included.

The primary objective of the trial is to evaluate an estimator of efficacy of the chemotherapy-light combination of glofitamab, polatuzumab vedotin and rituximab in patients with previously untreated aggressive large B-cell lymphoma not eligible for a fully dosed R-CHOP. The results shall be generated from the first 80 patients enrolled and can be used for initial effect estimation and planning of a subsequent phase III trial.

The secondary objectives of the trial are designed to i.) further characterize the outcome and, ii.) to evaluate the safety and tolerability of the chemotherapy-light combination R-Pola-Glo in patients with previously untreated aggressive large B-cell lymphoma not eligible for a fully dosed R-CHOP.

S9

The Registry of the European Mantle Cell Lymphoma Network (EMCL-R)

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Descriptive, non-interventional, pro- and retrospective clinical registry.

There is no investigational medical product. Neither is any treatment included into this protocol, nor will any advice be given for the treatment of an individual patient.

Population: All patients with the diagnosis of a MCL are eligible. Patients can be included regardless of their individual treatment time point during their disease course. Data of the prior disease course will be collected retrospectively.

Objective: It is the primary purpose to understand treatment algorithms, change of treatment patterns, influence of distinct treatment on the subsequent treatment lines, long-term results of clinical research projects, and patterns of resistance as well as health care utilization and understanding of patient related outcome parameters for a non-selected patient population. Subgroup analyses will be performed e. g. to understand the influence of specific novel treatment approaches and the fate of distinct risk populations, as defined by clinical, biologic or genetic characteristics or other known or new characteristics.

S10

AGMT metastatic Colorectal Cancer Registry (mCRC) – Third line and beyond

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This registry aims at retrospectively and prospectively evaluating the treatment landscape and clinical outcome of mCRC ≥ 3L in a collective attempt by including multiple oncologic centers in Austria.

The goal of this registry is to build a disease-specific registry aimed at assessing the therapeutic landscape of patients with mCRC ≥ 3L in Austria. It will be set up to collect real-world experience in the management of patients with this disease. This registry will collect data at various sites in Austria.

Population: The registry will be made available for all disciplines and physicians caring for cancer patients and will include patients ≥ 18 years with tissue-based diagnosis of mCRC after ≥ 2 prior lines of palliative systemic therapy including 5-FU, irinotecan, oxaliplatin, anti-VEGF, anti-EGFR (in case of RAS/BRAF wildtype), anti-PD1-therapy (in case of MSI/MMRd) in case of eligibility. About 500 patients will be included in this registry. This number may be revised over time as interest and demand dictates.

S11

MorningLyte: Study evaluating the efficacy and safety of mosunetuzumab plus lenalidomide in comparison to anti-CD20 monoclonal-antibody plus chemotherapy in subjects with previously untreated FLIPI-2-5 follicular-lymphoma

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This study is a phase III, randomized, open-label, international, multicenter, interventional trial, designed to compare the efficacy and safety of mosunetuzumab in combination with lenalidomide versus anti-CD20 monoclonal antibody (mAb) plus chemotherapy in patients with previously untreated FLIPI 2–5 follicular lymphoma.

This study is composed of a screening period (up to 6 weeks before randomization, i. e., up to 45 days, a treatment period (30 months i. e., 125w)), a safety follow-up period (90 days i. e., 3 months), and a survival follow-up period (up to 7 years after the last randomized patient). The enrollment will last approximately 34 months. The total duration of the study will be therefore approximately 10 years.

All randomized patients will be followed for progression-free survival and overall survival using the same schedule. Patients will be followed up from End of treatment evaluation every 3 months during the first two years, then every 6 months during the next 3 years, then yearly until the end of study.

The end of study will occur when all randomized patients have been followed-up for survival for at least 7 years (or discontinued study early).

Primary Efficacy Objective: To demonstrate the superiority of mosunetuzumab + lenalidomide combination versus anti-CD20 mAb plus chemotherapy with regards to Progression Free Survival (PFS) in previously untreated patients with International Prognostic Index (FLIPI) 2–5 Follicular Lymphoma.

S12

AGMT Austrian Lymphoma Registry

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This registry is designed as international multicenter observational cohort of patients with lymphoma. Information on patient's clinical presentation, tests, diagnosis, and treatment will be obtained through extraction of data from existing patient medical charts. Longitudinal follow-up data, including survival and tumor progression, will also be extracted from patient medical charts. This patient follow-up data will be obtained until patient death or loss to follow-up.

The goal of this registry is to build a disease-specific registry aimed at assessing the therapeutic landscape of patients with lymphoma in Austria. It will be set up to collect real-world experience in the management of patients with this disease. This registry will collect data at various sites in (and outside) Austria. The aim is to gain valuable insights on both efficacy and toxicity, as well as the sequence of use of various treatments in a routine clinical setting.

Population: Interested sites that treat patients in this indication will be invited to participate in this registry. The registry will include patients ≥ 18 years (at time of consenting) with lymphoma. About 4000 patients will be included in this registry. This number may be revised over time as interest and demand dictates.

S13

Safety and tolerability data on Kedrion's 5 % IVIG – A twenty-seven years (1997–2024) pharmacovigilance database analysis

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Introduction and Aims: Intravenous immunoglobulins (IVIg) are used to treat a variety of immune disorders, in particular primary and secondary immunodeficiency and several autoimmune diseases. The aim of this analysis is to describe tolerability and safety of Kedrion 5% IVIg over a 25-year time span.

Methods: The source data refers to the period January 1997–26 February 2024 and is retrieved from the Kedrion Pharmacovigilance Database (Veeva Vault safety). The total number of doses is calculated assuming an average dosage of 0.4 g/Kg and an average body weight of 70 kg.

Results: 988 ADRs are reported in patients receiving Kedrion's 5% IVIG (42.7% in males, 46.8% in females, 10.5% gender not reported; 61.9% in adults, 21.4% in pediatrics and 16.6% not specified).

Out of 3,164,850 estimated doses distributed worldwide, a total of 998 ADRs were received by Kedrion (a reporting rate of 3.15 ADRs/10,000 infusions) of which 43% (429/998) non-serious and 57% (569/998) serious. The most frequent (≥2%) reported ADRs are: headache ($n=87$), pyrexia ($n=51$), urticaria ($n=37$), rash ($n=36$), erythema ($n=26$), chills ($n=25$), hypertension ($n=22$), dyspnoea ($n=20$).

In particular, 33 thromboembolic events (TEEs), 18 cases of hypersensitivity, 16 cases of aseptic meningitis, 3 cases of transfusion related acute lung injury (TRALI), and 12 cases of hemolysis have been reported since 1997 up to end of February 2024.

Conclusions: Based on spontaneous and literature reporting safety rate over the more than 27 years, the benefit-risk balance of Kedrion 5% IVIG is to be considered favourable.

S14

A Prospective non-interventional study of trastuzumab deRuxtecan for patients with advanced HER2-pOsitive gaStric or gastroesoPhageal junction adEnocarcinoma who have Received a prIor Trastuzumab-based regimen (PROSPERITY)

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Background: Trastuzumab deruxtecan (T-DXd) is approved as monotherapy for the treatment of adult patients with advanced HER2-positive advanced GC or GEJ adenocarcinoma who have received a prior trastuzumab-based regimen. Results on T-DXd treatment in HER2-positive advanced GC or GEJ adenocarcinoma have so far been limited to clinical trials and the insight into real world data is limited.

Aim: This non-interventional study will provide real-world insight into T-DXd treatment for HER2-positive gastric or GEJ adenocarcinoma with data on effectiveness, safety and tolerability, patient-reported outcomes, treatment patterns, geriatric health status and HER2 testing. In addition, data in HER2-positive patients treated with conventional therapy other than T-DXd as further line treatment will be collected.

Method: PROSPERITY (NCT05993234) is a multi-center, multi-country, observational, prospective, non-interventional study planning to enroll 257 patients from 79 sites in 5 European countries (Austria, Belgium, Germany, Italy, and Portugal) receiving T-DXd or conventional therapy as their routine clinical care for advanced HER2-positive gastric or GEJ adenocarcinoma patients will be followed up for approximately 31 months. It is anticipated that 45 patients (15 patients treated with conventional therapy/30 patients treated with T-DXd) will be enrolled in 15 sites in Austria. The primary parameter is the time to next treatment, secondary objectives include effectiveness, safety and tolerability as well as patient reported outcomes.

Conclusion: PROSPERITY will be beneficial for improving guidance to maximize patient treatment as a non-interventional longitudinal gastric and GEJ adenocarcinoma study.