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Return to work trajectories after early breast cancer diagnosis: A population-based cohort study in the French National Healthcare Insurance database.

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explore the possible associations between these parameters and clinical outcomes in non-small-cell lung cancer (NSCLC) pts receiving first-line Pembrolizumab monotherapy.

Methods: A retrospective review of consecutive advanced NSCLC pts treated with Pembrolizumab as first-line therapy at two academic medical institutions from August 2017 to October 2021 was performed. The estimation of skeletal muscle and adipose tissue were performed using pre-treatment computed tomography scans at the level of the third lumbar vertebra, obtaining Skeletal Muscle Area (SMA), Intermuscular Adipose Tissue (IMAT), Subcutaneous Adipose Tissue (SAT), and Visceral Adipose Tissue (VAT). Data were correlated to progression-free/overall survival (PFS/OS) using a Cox and logistic regression model. Log-Rank analysis was used for Kaplan-Meier curves comparison.

Results: Data from 102 pts (median age: 68 years [range 36-85]; median follow-up: 12 months [range 1-131]) were collected. Overall, 52% and 58.8% of pts met established radiographic criteria for evidence of sarcopenia and myosteatosis, respectively, which occur across the BMI spectrum. Median OS was 17.2 months; higher SAT (HR 1.01, 95% CI 1.00-1.02; $p=0.017$) and higher VAT/SMA ratio (HR 1.48, 95% CI 1.07-2.05; $p=0.016$) were significantly associated to OS. A ROC curve was constructed to obtain a VAT/SMA ratio cut-off for OS.

Conclusions: Our findings showed that pre-treatment skeletal muscle wasting was often reported in NSCLC patients undergoing Pembrolizumab, across all BMI categories. Besides, our preliminary results support the hypothesis that BC may affect these patients' survival, suggesting a potential interaction between BC and the immune system. Further analyses are ongoing in this patients' cohort, to augment knowledge in this field combining biological and clinical features with analytic and preclinical studies.

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1619P Assessment of the pharmacokinetic interaction of enzalutamide with oxycodone in men with prostate cancer: The ENZYME study

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Background: Up to 90% of patients with castration-resistant prostate cancer (CRPC) will develop symptomatic metastases requiring pain medication. Oxycodone is an opioid metabolized primarily by cytochrome P450 (CYP) 3A4 to the inactive metabolite noroxycodone and by CYP2D6 to the active metabolite oxymorphone. Both are further metabolized to noroxymorphone by CYP3A4 and 2D6. Enzalutamide (ENZ) is a widely used androgen receptor antagonist for the treatment of CRPC and a strong inducer of CYP3A4. Due to this CYP3A4 induction, it is expected that ENZ will reduce the analgesic effects of oxycodone. This is the first study investigating the effect of ENZ on the pharmacokinetics of oxycodone.

Methods: We performed a prospective, two-arm parallel study in men with prostate cancer. Patients in arm 1 were treated with ENZ 160 mg once daily for at least 40 days; patients in control arm 2 were not treated with ENZ. All patients received a single oral dose of 15 mg normal-release oxycodone, followed by blood sampling up to 8 hours after dosing. Plasma concentrations of oxycodone, noroxycodone, oxymorphone and noroxymorphone were quantified using a validated LC-MS/MS method. The difference in geometric mean of the maximum plasma concentration (C_{max}) and area under the curve (AUC_{0-8h}) between the arms was determined.

Results: In total 27 patients were included, of who one subject was excluded since he was a CYP2D6 poor metabolizer. In the ENZ arm ($n=13$), mean AUC_{0-8h} and C_{max} of oxycodone were resp. 44.7% ($p<.001$) and 35.5% ($p=.004$) lower compared to the control arm ($n=13$). ENZ decreased AUC_{0-8h} and C_{max} of the active metabolite oxymorphone with resp. 74.2% ($p<.001$) and 56.0% ($p=.001$). In contrast, ENZ increased AUC_{0-8h} and C_{max} of the CYP3A4-dependent inactive metabolite noroxycodone with resp. 61.2% ($p=.001$) and 78.2% ($p=.001$) and of the inactive metabolite noroxymorphone with resp. 45.0% ($p=.032$) and 59.8% ($p=.027$).

Conclusions: ENZ decreases exposure to oxycodone and its active metabolite oxymorphone. This interaction is clinically relevant because pain may not be adequately controlled and there is a risk of overdose upon ENZ discontinuation. A switch to an opioid that is not metabolized by CYP3A4, e.g. morphine, may be necessary to achieve adequate and safe pain management during treatment with ENZ.

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1620P Return to work trajectories after early breast cancer diagnosis: A population-based cohort study in the French National Healthcare Insurance database

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Background: Return to work (RtW) is important for quality of life after breast cancer (BC), and a difficult challenge for many patients (pts). Current evidence relies mainly on selected populations and limited indicators. We aimed to construct RtW indicators based on sickness leave (SL) and disability pension (DP) benefits, and to explore RtW trajectories.

Methods: We conducted a retrospective cohort study using data from a random sample of 1/97th beneficiaries of the French National Health System. All women aged 25-55 years with a first early BC diagnosis between 2013 and 2016 were included and followed-up for 3 years. We constructed RtW indicators based on literature review, data availability and stakeholders' expertise in the national context. Descriptive analyses were performed on sample characteristics and RtW indicators. Longitudinal RtW trajectories were explored using sequence analysis and clustered using optimal matching.

Results: Data from 306 pts (56% HR+/HER2-, 24% triple-negative, 14% HER2+, 6% in situ) were extracted. (Neo)adjuvant chemotherapy, trastuzumab and endocrine therapy were administered in 59%, 14% and 66% of pts, respectively. Median time with compensation until full and sustainable (> 28 days) RtW was 242 days. Median cumulative lengths of all-type and full-time sickness absence during follow-up were 450 days and 313 days, respectively. Full-time or partial RtW was achieved by 57% of pts at 1-year, 82% at 2-year and 85% at 3-year after diagnosis. Three RtW trajectories were identified: "RtW within a year" (48% of the population) with pts experiencing RtW during the 1st year and limited subsequent work interruption, "RtW supported by partial SL or DP" (38%) with pts typically returning to work during the 2nd year after a partial SL period or with a partial DP, and "continued compensation" (14%) with pts receiving either complete SL benefit or DP at 3-year.

Conclusions: Identification of RtW trajectories based on French medico-administrative databases seems feasible. It revealed large individual variability and identified three distinct groups of RtW trajectories. Further exploration of trajectory determinants and lived experience is needed to develop targeted RtW interventions.

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1621P miRNA signature as early predictor of hyponatremia and survival in lung cancer: Preliminary results from the ISA retrospective study

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Background: Syndrome of inappropriate antidiuresis (SIAD) in cancer is the main cause of hyponatremia and is associated with poorer survival, hospitalization and health costs in lung cancer (LC) patients (pts). Micro-RNAs (miRNAs) represent promising biomarkers with therapeutic potential. Our retrospective study aims to