Methods. This study was conducted from the Brazilian payer perspective according to local guidelines, with a lifetime horizon. The use of SIRT in patients with intermediate- or advanced-stage HCC, without extrahepatic disease and ineligible to transarterial chemoembolization, was compared with sorafenib, the commonly used HCC systemic treatment in Brazil. A sensitivity analysis included the subgroup of patients with low tumour burden and preserved liver function.

A partitioned-survival model was developed, which included a tunnel state for patients downstaged to receive a treatment with a curative intent such as liver surgery, transplantation or ablation. Survival curves, utilities and adverse events incidence were extracted from published sources of pivotal randomized control trials. Effectiveness of health interventions was measured in quality-adjusted-life-years (QALYs) and life-years (LYs). Local costs from Brazil were applied. Future costs and effects were discounted at five percent. A willingness-to-pay threshold of USD 53,936 was used, based on a 2017 review of healthcare technology adoption in Brazil.

Results. LYs and QALYs were higher for SIRT using Y-90 resin microspheres versus sorafenib (0.27 and 0.20 incremental LYs and QALYs, respectively) and costs were slightly higher for SIRT (USD 3,056 incremental costs). The incremental cost-effectiveness ratio (ICER) was USD 14,948 per QALY in the basecase.

One-way and probabilistic sensitivity analyses confirmed the robustness of the analyses. Scenario analyses tested different model assumptions and reinforced the basecase results indicating that SIRT using Y-90 resin microspheres was highly likely to be cost-effective compared with sorafenib. Also, the ICER was lower in the subgroup compared with the overall population.

Conclusions. SIRT using Y-90 resin microspheres represents a cost-effective option compared with sorafenib in Brazil.

PD29 Systematic Review With Meta-analysis Of Pharmacokinetic Parameters Of Tyrosine Kinase Inhibitors Used In Chronic Myeloid Leukemia

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Introduction. Therapeutic drug monitoring (TDM) is a cost-effective tool to increase treatments' efficacy and safety. Analyses of pharmacokinetics proprieties of tyrosine kinase inhibitors (TKI) used for chronic myeloid leukemia (CML) can contribute towards effective TDM, development of tailored treatments and new dosing regimens. We aimed to synthesize the available evidence on pharmacokinetic parameters of imatinib, nilotinib, bosutinib, ponatinib in healthy individuals vs. CML patients.

Methods. Systematic searches were conducted in PubMed, Scopus and Web of Science. We included in vivo studies addressing TKIs' pharmacokinetics, including maximum observed concentration (Cmax), time of maximum observed concentration (Tmax) and half-life (t1/2). Meta-analyses of event rates (mixed-effect models) were performed for the parameters of interest: area under the concentration-time curve from time zero to the last measurable concentration (AUC0-t) and from time zero to infinity (AUC 0-∞). Results were presented as event rates with 95 percent confidence intervals. Heterogeneity was assessed using chi-square and I2 statistical tests and considered significant when p<0.05 and high when I2>75 percent (Comprehensive Meta-Analysis v.2 Biostat-Englewood, NJ).

Results. Overall, 50 articles were included for analyses (n=26 imatinib, n=11 nilotinib, n=8 bosutinib, n=5 ponatinib). Most studies were performed in the United States (46.0%), designed as open-label trials (70.0%). Several significant interactions between TKI with enzyme inhibitors (ketoconazole, midazolam, aprepitant, metoprolol, grapefruit juice), proton pump inhibitors (esomeprazole, lanzoprazole, omeprazole), antacids, H2 antagonists (famotidine) and enzyme inducers (St. John's, rifampicin) were found (p<0.001). Given the significant increase in AUC and Cmax in patients with hepatic/liver impairments currently using TKI, strict therapeutic monitoring is paramount to maintain safety. The between study heterogeneity was rated as moderate to high (I2=75-90%) due the limited number of trials for some drugs, different study design, and populations.

Conclusions. The co-administration of TKI with hepatic enzyme inducers or inhibitors, proton pump inhibitors, antacids, H2 antagonists, as well as in patients with hepatic/liver failures requires caution and additional monitoring. Further well-designed trials are needed to strengthen this evidence for some TKIs, namely bosutinib and ponatinib.

PD30 Radioactive Seed Localization And Radio-Guided Occult Lesion Localization For Non-Palpable Breast Cancer Surgery: A Meta-Analysis

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Introduction. Non-palpable breast cancers require intraoperative localization to guide the surgical procedure. The radio-guided occult lesion localization (ROLL) and radioactive seed localization (RSL) techniques use radioactive material (technetium-99m labeled macroaggregated albumin and iodine-125 seeds, respectively) implanted at the lesion site. The success of conservative surgery depends on complete tumor excision with negative surgical margins. The objective of this study was to perform a meta-analysis of the surgical effectiveness of the ROLL and RSL techniques with respect to rates of positive surgical margins, reoperation, and recurrence.

Methods. A systematic search of the PubMed, Embase, LILACS, SciELO, and Web of Science databases was performed on 2 August 2021. A standard form was used to extract data from the studies selected in the screening process. The ROBINS-I tool was used to analyze risk of bias and RevMan 5.4 software was used to perform the meta-analysis.

Results. Four observational studies met the inclusion criteria. The overall evidence quality was moderate. The studies included women aged from 28 to 91 years with non-palpable breast cancer. The results demonstrated similar effectiveness between RSL and ROLL for rates of positive surgical margins (risk ratio [RR] 0.83, 95% confidence interval [CI]: 0.50, 1.39; 763 patients) and reoperation (RR 1.14, 95% CI: 0.75, 1.74; 1,550 patients). Regarding the rate of disease recurrence, RSL was superior to ROLL (RR 0.50, 95% CI: 0.29, 0.87; 939 patients).

Conclusions. The results demonstrate that the ROLL and RSL techniques are equivalent with respect to rates of positive surgical margins and reoperation, although patients undergoing RSL had lower rates of disease recurrence. However, there is a tendency to favor the RSL technique because of the longer interval between implantation and surgery, which is possible due to the longer half-life of iodine-125 (59.4 days). This also means that radioactive seed implantation can occur before neoadjuvant chemotherapy, so the tumor bed remains marked if further interventions are required, obviating the need for another invasive procedure before surgery.

PD32 Cost-Utility Of Selective Internal Radiation Therapy Using Y-90 Resin Microspheres For Chemotherapy-Refractory Metastatic Colorectal Cancer In Brazil

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Introduction. There were an estimated 55,102 new cases of colorectal cancer (CRC) in Brazil in 2020, comprising 9.3 percent of all newly diagnosed cancers, and making it the third most common cancer in the Brazilian population. Up to half of all patients with CRC will develop liver metastases, and the prognosis for these patients is poor. The objective of the present analysis was to evaluate the cost-utility of selective internal radiation therapy (SIRT) using Y-90 resin microspheres versus best supportive care (BSC) in patients with unresectable, liver-dominant, chemotherapy-refractory metastatic CRC (mCRC).

Methods. A three-state partitioned survival model was developed in Microsoft Excel to evaluate the cost-utility of SIRT using Y-90 resin microspheres versus BSC. Membership of the three model states of pre-progression, post-progression and death was governed by parametric models of Kaplan-Meier data from a retrospective, interventional study. Costs associated with SIRT using Y-90 resin microspheres, BSC, and adverse events were obtained from Brazilian

sources and reported in 2021 United States dollars (USD). Future costs and effects were discounted at 5 percent. One-way and probabilistic sensitivity analyses (PSA) were performed. A willingness-to-pay threshold of USD 53,936 was used based on a 2017 review of Brazilian healthcare technology adoption.

Results. The base case analysis showed that Y-90 resin microspheres would result in an increase of 0.76 QALYs versus BSC, increasing quality-adjusted life expectancy from 0.67 QALYs to 1.43 QALYs. The improvement in quality-adjusted life expectancy was accompanied by an increase in costs from USD 9,884 to USD 40,399 over the model time horizon, corresponding to an increase of USD 30,515, and yielding an incremental cost-utility ratio (ICUR) of USD 40,265 per QALY gained. PSA showed there was a 90.8 percent likelihood of cost-effectiveness at USD 53,936 per QALY gained.

Conclusions. SIRT using Y-90 resin microspheres was cost-effective versus BSC in the treatment of unresectable, liver-dominant mCRC patients and should be considered for incorporation in the Brazilian Private Healthcare System.

PD33 Development And Validation Of A Machine Learning-Based Prediction Model For COVID-19 Diagnosis Using Patients' Metabolomic Profile Data

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Introduction. We aimed to develop and validate machine learning (ML) -based algorithms to predict COVID-19 diagnosis as well as to identify new biomarkers associated with the disease.

Methods. Initially, 96 blood samples of patients diagnosed with COVID-19 (Thaizhou Hospital, China) were analyzed through liquid chromatography coupled to mass spectrometry. Samples of patients presenting other pneumonias or severe acute respiratory syndrome, but with negative RT-PCR for SARS-CoV-2, were used as positive controls. Samples from healthy volunteers were used as negative controls. The final database included around 1000 metabolites. Exploratory analyses for the development of ML-based models using principal component analysis (PCA) were performed. Leverage plot versus studentized residuals method was used to detect outliers. Three supervised ML-based models were developed: discriminant analysis by partial least squares (PLS-DA), artificial neural networks discriminant analysis (ANNDA) and k-nearest neighbors (KNN). Samples for the training (70%) and testing sets (30%) were randomly selected using the Kenrad Stone algorithm. Models' performance was evaluated considering accuracy, sensitivity and specificity. Analyses were conducted in SOLO (Eigenvector-Research).