Methods: This is an observational, retrospective, single center study. A total of 150 Brazilian pts diagnosed with conventional CS between 2002 and 2024, with available fresh or FFPE tumor tissue, are expected to be included. In this report, hotspot mutations in *IDH1* (R132), *IDH2* (R172), and *TERT* (c.-124C>T and c.-146C>T) were analyzed using multiplex PCR followed by NGS. A retrospective chart review was conducted to collect clinical data. Overall survival (OS) and relapse-free survival (RFS) were estimated using the Kaplan-Meier method.

Results: This partial analysis included 85 pts (46 males, 54.1%; 39 females, 45.9%), with a median age of 44 years (range 11—80). Tumor locations included the pelvis (30.6%), lower limbs (10.6%), and rib cage (3.5%). Tumor grades were 1 (51.8%), 2 (38.8%), and 3 (9.4%). Only 3.5% of pts had metastases at diagnosis. *IDH1* mutation was identified in 32.9% of cases, *IDH2* mutation in 9.4%, *TERT* c.-124C>T mutation in 24.7% and *TERT* c.-146C>T mutation in 1.2%. Coexisting *IDH1+TERT* mutations were observed in 9 cases, and *IDH2+TERT* in 5 cases. The mutations were more frequent in appendicular skeleton tumors (*IDH1* 71.4%, *IDH2* 100%, *TERT* 90.5%), though without statistical significance (p = 0.37, 0.09, 0.08, respectively). Median follow-up was 72 months (95% CI 57.7 − 86.3). OS was not reached. Five-year OS was 100% for *IDH1*-mutated (mut) vs. 91% for *IDH1*-wild-type (wt) (p=0.7), 50% for *IDH2*-mut vs. 98% for *IDH2*-wt (p=0.0001), and 81% for *TERT*-mut vs. 97.5% for *TERT*-wt (p=0.1). RFS was 27 vs. 42 months for *IDH1*-mut vs. -wt (p=0.3), 13 vs. 34 months for *IDH2*-mut vs. -wt (p=0.3), and 29 months for both *TERT*-mut and -wt (p=0.7).

Conclusions: Preliminary data indicate lower mutation rates in *IDH1*, *IDH2*, and *TERT* in this Brazilian cohort compared to prior reports. These mutations were more frequently observed in appendicular CS. Additional cases will be analyzed to validate these findings.

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2749eP Navigating regulatory complexity in combined studies under clinical trial and in vitro diagnostic regulations: Lessons from the CHONQUER study on molecular pre-screening for IDH1 mutation in chondrosarcoma

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Background: CHONQUER is a Phase 3 clinical trial of Ivosidenib for patients with IDH1-mutated chondrosarcoma under the 536/2014 Clinical Trial Regulation (CTR). No CE-marked In Vitro Diagnostics (IVDs) exist to identify eligible patients. Therefore, the trial runs in parallel with a performance study of an investigational IVD under the 2017/746 In Vitro Diagnostic Regulation (IVDR). As the EUDAMED platform is not yet fully functional, performance studies are authorized under national requirements. Although trial approval via the Clinical Trial Information System was granted in November 2024, performance studies approval was delayed due to IVDR-specific hurdles, particularly the need for a Performance Study Application (PSA) detailing molecular pre-screening for IDH1 mutation.

Methods: A retrospective analysis evaluated the regulatory and operational impact of the PSA across six EU Member States (Belgium, France, Germany, Italy, Spain, The Netherlands), using feedback from sponsors, competent authorities (CAs), ethics committees (ECs), sites, and CROs to identify key challenges and propose mitigation strategies.

Results: EU site activation occurred at least six months after Clinical trial authorization (CTA) due to PSA-requirements. Unlike non-EU countries, EU implementation was delayed by inconsistent IVDR interpretations across Sponsor, CAs and ECs. Challenges included CTA and PSA timeline differences and varied national submission strategies. Additional requirements included performance study-specific ICFs, CTA ICF amendments, duplicative forms, investigator requirements, and translations.

Conclusions: The PSA processes under IVDR and associated timelines need to be considered carefully when planning global trials involving products regulated under both CTR and IVDR. A harmonized approach, such as Article 74's coordinated assessment, could improve efficiencies. The implementation of EUDAMED's centralized system could harmonize processes and expedite patients getting quicker access to clinical trials evaluating innovative drugs.

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2750eP Molecular tumor boards (MTB) as a tool for phase I and II clinical trial (CT) selection in sarcoma: A 5-year retrospective study

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Background: Sarcomas have a broad spectrum of molecular alterations, offering opportunities for novel therapeutics. However, the rarity and diversity of its subtypes make large-scale CTs challenging. Therefore, early-phase CTs are critical. This retrospective study evaluates the role of MTB in selecting patients with sarcoma for phase 1 and 2 CTs.

Methods: We performed a retrospective analysis reviewing data from 2020 to 2024 for patients with sarcoma presented at the MTB of the Department of Investigational Cancer Therapeutics at the University of Texas MD Anderson Cancer Center. The MTB includes oncologists, molecular biology experts, and CT coordinators. CT options were selected by the MTB based on CT eligibility criteria, molecular annotations and clinical expertise. Patients could be presented one or multiple times throughout their disease course. This study aims to assess the MTB recommendations, subsequent patient enrollment in CT and overall survival (OS) from time of presentation at MTB.

Results: A total of 288 patients were presented in the MTB, including 8 with gastrointestinal stromal tumors, 48 with bone sarcoma, and 232 with soft tissue sarcoma. Over half of the patients (51.4%) were enrolled in CTs within the department at some point during their disease course. The 288 patients were presented at the MTB a median of 1.38 times per patient between 2020-2024, for a total of 397 presentations. The number of presentations was 66 in 2020, 69 in 2021, 77 in 2022,