Table: 77P Treatment within each study arm

Study arm	6 week RT period	1 year consolidation period
CONCORDE-A	Olaparib+RT RT only	No treatment
CONCORDE-B	AZD1390+RT RT only	
CONCORDE-C	Ceralasertib+RT RT only	Cerelasertib + durvalumab Durvalumab
CONCORDE-E	AZD5305+RT RT only	Durvalumab

Results: CONCORDE opened to recruitment in April 2021. Recruitment was initially slow, resulting in limited data to inform dose escalation decisions. 10 patients were recruited to the RT only arm after 9 months across the arms, with a DLT rate of 10%. This was comparative to the expected DLT rate of 25% and randomisation allocation was changed to 3:1. As of 01/11/23 20 RT only patients have been treated, with a current DLT rate of 6% (95%CI: 0.1-27.3%), in line with prior expectations.

Conclusions: Pooling RT only patients across arms to estimate DLT rates presents a useful concurrent comparator to put the estimated DLT rate for informing dose escalation into context, and the rate in RT+DDRi patients to help attribute toxicity to the combination of DDRi and thoracic RT. The platform design necessitates fewer comparator patients, compared with multiple standalone comparison design trials.

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Legal entity responsible for the study: University of Leeds.

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78P Implementing the modified partial order time-to-event continual reassessment method in a phase I ovarian cancer combination trial with unknown dosing ordering

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Background: When investigating multiple agents, pairs of combination doses may initially have unclear toxicity probability orderings. The partial order continual reassessment method (PO-CRM) design was initially proposed to evaluate combination doses with unknown ordering. It was later extended to cope with late-onset toxicities by incorporating both full and partial dose-limiting toxicity (DLT) follow-up, thereby avoiding impractically long trial durations. This work shares insights from applying a novel tailored PO-TITE-CRM design in a phase I ovarian cancer combination trial to identify the maximum tolerated dose (MTD) for two DNA damage response inhibitors.

Methods: To implement the PO-TITE-CRM design, statistical parameters were calibrated considering expected DLT occurrence distribution, whilst minimising the trial duration. With up to 18 DLT evaluable patients, the model selects the toxicity ordering with the highest posterior probability among the available treatment combinations, and then adaptively allocates the dose with estimated DLT rate closest to the 25% target rate to the next patient. Extensive simulations assessed model performance across varied toxicity profiles, executed by modifying codes from R packages pocrm and dfcrm.

Results: We highlight our collaborative development of a customised PO-TITE-CRM, strategically incorporating the nuanced expected tolerability profile of the combination therapy and operational factors. Simulation results demonstrate that trial duration can be substantially reduced compared to PO-CRM design, by enabling semi-continuous accrual, without compromising on patient safety and the accuracy of MTD recommendations.

Conclusions: These findings underscore the practical utility of the PO-TITE-CRM, showing its adaptability to individual trial needs. The approach holds promise in accelerating dose-finding combination trials despite the challenge of unknown ordering. It highlights the vital role of close collaboration with the trial teams in designing and delivering innovative dose-finding trials, essential for promoting the adoption of these methodologies.

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79P Pharmaceutical cost savings for the treatment of oncology patients in clinical trials

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Background: The development of new therapies does not stop, which is reflected in the fact that between 2011 and 2016, 68 new molecules have been approved for 22 different oncological indications and has a direct impact on increased survival. However, coupled with this success, there has been a substantial increase in the cost to a level that, currently, is causing serious problems to be assumed by the different Public Administrations. Among the measures to support this incipient health expenditure there are price-volume agreements, maximum spending ceilings, maximum cost per patient and/or period or shared risk agreements, but we must not forget that clinical trials can be a tool that facilitates financial sustainability. of the health system.

Methods: The aim of this study was twofold: to assess the annual pharmaceutical savings associated with the treatment of cancer patients at the Marqués de Valdecilla University Hospital during the clinical trials conducted throughout 2020, and to estimate the cost of innovative antineoplastic therapies unapproved by the Spanish Agency for Medicines and Health Products that patients receive as experimental treatment in a clinical trial. An observational and financial analysis of the drug cost savings was applied. Each clinical trial and the characteristics of the pathology were analyzed and matched with a therapeutic alternative. Direct cost savings to the Regional Health System of Cantabria were measured, related to clinical trials. The cost of innovative therapies used as an experimental treatment in clinical trials was also quantified as an investment.

Results: This study includes 38 clinical trials with a sample of 101 patients. The findings indicate that overall, all the clinical trials analyzed provide a total cost savings of €603,350.21 and an average cost saving of €6,630.22 per patient. Furthermore, the final investment amounts to €789,892.67, with an average investment of €15,488.09 per patient.

Conclusions: This study demonstrates that clinical trials are essential for the advancement of science. Furthermore, clinical trials can be a significant source of income for both hospitals and Regional Health Systems, contributing to their financial sustainability.

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