3. RELAPSED/REFRACTORY MULTIPLE MYELOMA

RANDOMIZED PHASE II DOSE OPTIMIZATION STUDY OF INOBRODIB (CCS1477) IN COMBINATION WITH POMALIDOMIDE AND DEXAMETHASONE IN RELAPSED/REFRACTORY MULTIPLE MYELOMA

E. Searle[1], V. Campbell[2], C. Pawlyn[3], D. Vogl[4], S. Holstein[5], S. Gooding[6], M. Jenner[7], T. Creasey[8], A. Chaidos[9], P. Rodríguez-Otero[10], F. Al-Kaisi[11], A. Brearton[12], S. Moore[6], J. O'Nions[13], T. Somervaille[1], T. Knurowski[14], K. Clegg[14], S. Paul[14], K. Frese[14], N. Joseph[15]

[1]The Christie NHS Foundation Trust, Manchester, UK; [2]Western General Hospital, Edinburgh, UK; [3]The Royal Marsden NHS Foundation Trust, London, UK; [4]Hospital of the University of Pennsylvania, Philadelphia, USA; [5]University of Nebraska Medical Center, Omaha, USA; [6]Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [7]University Hospital Southampton NHS Foundation Trust, UK; [8]Northern Centre for Cancer Care, Newcastle upon Tyne, UK; [9]Imperial College Healthcare NHS Trust, London, UK; [10]Clínica Universidad de Navarra, Pamplona, Spain; [11]Royal Derby Hospital, UK; [12]The Clatterbridge Cancer Centre, Liverpool, UK; [13]University College London Hospital, UK; [14]CellCentric Ltd, Cambridge, UK; [15]Emory Winship Cancer Institute, Atlanta, USA

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Background. Inobrodib (CCS1477; Ino) is a first-in-class, potent, selective, orally bioavailable inhibitor of the bromodomains of p300 and CBP, histone acetyltransferases with oncogenic roles in haematologic malignancies. Inobrodib demonstrates anti-tumor activity in multiple myeloma cell lines and synergistic activity with pomalidomide (Pom). The combination of Ino with pomalidomide and dexamethasone (dex; InoPd) has previously shown manageable safety and clinical activity in heavily pretreated relapsed/refractory multiple myeloma (RRMM).

Methods. Eligible patients with RRMM had exhausted standard-of-care options or received ≥2 prior therapies including lenalidomide and a proteasome inhibitor (if pomalidomide-naïve). Patients were randomized to inobrodib 20 mg, 30 mg, or 40 mg twice daily on a 4-days-on/3-days-off schedule, combined with pomalidomide 4 mg and dexamethasone 20–40 mg (age-dependent), administered in 28-day cycles. Randomization was stratified by prior pomalidomide exposure. Adverse events were graded per CTCAE v5.0 and responses were Investigator-assessed using IMWG criteria.

Results. At a data cutoff of 6 October 2025, 61 patients were enrolled. Median age was 70 years (range 44–83), and 79% had ECOG performance status <1. Thirty-six percent had high risk disease by IMWG Consensus Genomic Staging. The median number of prior therapies was 5 (range 2–17); 53% were pomalidomide-refractory, 71% were triple--class refractory, and 66% had received prior BCMA- or T--cell engager–directed therapy. Grade 3/4 treatment-emergent adverse events occurred in 71% of patients and were predominantly haematologic (neutropenia 34%, thrombocytopenia 36%, anemia 20%). Thrombocytopenia was the primary overlapping toxicity; at the 20-mg dose, its frequency and severity were comparable with published pomalidomide/dexamethasone data. Among 44 response-evaluable patients, overall response rates were 69%, 54%, and 33% in the 20-, 30-, and 40-mg cohorts, respectively. High response rates were observed in a high-unmet-need population (pomalidomide-refractory and post-BCMA/T-cell engager patients), with 60% and 75% ORR in the 20-, and 30-mg cohorts, respectively. Overall, the 20-mg dose demonstrated the most favorable benefit–risk profile.

Conclusions. InoPd demonstrates a manageable safety profile and promising clinical activity in heavily pretreated RRMM. Initial results support selection of the 20-mg dose for future registrational studies. Additional trial arms evaluating inobrodib in combination with elranatamab and teclistamab are ongoing.