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P863 AN OPEN-LABEL PHASE I/IIA STUDY TO EVALUATE THE SAFETY AND EFFICACY OF CCS1477 AS MONOTHERAPY AND IN COMBINATION WITH POMALIDOMIDE/DEXAMETHASONE IN RELAPSED/REFRACTORY MULTIPLE MYELOMA

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

Emma Searle*[1,2], Jim Cavet[1,2], Steven Knapper[3], Ceri Bygrave[4], Victoria Campbell[5], Dima El-Sharkawi[6], Charlotte Pawlyn[6,7], Maria Creignou[8], Harriet S. Walter[9,10], David Valcarcel[11], Marta Hidalgo[11], Tomasz Knurowski[12], Karen Clegg[12], Neil Pegg[12], Will West[12], Debbie Haynes[12], Kristopher Frese[12], Tim C. P. Somervaille[1,2,13]

[1]The Christie Nhs Foundation Trust, Manchester, United Kingdom; [2]The University Of Manchester, Manchester, United Kingdom; [3]Cardiff University, Cardiff, United Kingdom; [4]University Hospital Wales, Cardiff, United Kingdom; [5]Western General Hospital, Edinburgh, United Kingdom; [6]The Royal Marsden Nhs Foundation Trust, London, United Kingdom; [7]The Institute Of Cancer Research, London, United Kingdom; [8]Karolinska University Hospital, Stockholm, Sweden; [9]University Hospitals Leicester, Leicester, United Kingdom; [10]University Of Leicester, Leicester, United Kingdom; [11]Vall D'Hebron Institute Of Oncology, Barcelona, Spain; [12]Cellcentric Ltd, Cambridge, United Kingdom; [13]Cancer Research Uk Manchester Institute, Manchester, United Kingdom

Background:

Inobrodib (CCS1477) is a first in class potent, selective, and orally bioavailable inhibitor of the bromodomains of p300 and CBP, two closely related histone acetyl transferases with oncogenic roles in hematological malignancies. Inobrodib exhibits potent anti-tumor cell activity in a range of hematological cell lines, including multiple myeloma, and demonstrated additive/synergistic activity with pomalidomide.

Aims:

We report preliminary safety (primary objective), efficacy (secondary) and PK data for inobrodib both alone and in combination with pomalidomide (POM) and dexamethasone (DEX) in patients (pts) with relapsed/refractory multiple myeloma (RRMM) treated in this Phase I/IIa trial (NCT04068597).

Methods:

Eligible pts who consented had confirmed RRMM and had exhausted available standard of care treatment options (81% of patients were triple class exposed). During monotherapy dose escalation, pts received inobrodib in 28-day cycles at doses ranging 25-50 mg either OD or BD on a continuous or intermittent schedule. During combination dose expansion, pts received POM and DEX as per the approved dosing schedule, in addition to inobrodib on an intermittent schedule. Adverse events (AEs) were graded by CTCAE v5.0. Responses were investigator assessed per IMWG.

Results:

Overall, 32 RRMM pts with a median age of 67 yrs (range 50-90) received inobrodib monotherapy. The median prior lines of therapy was 7 (range 4-9). Median follow-up was 42 days (range 2-308), with a median number of 1.5 cycles received (range 0.25-10).

Grade (Gr) 3/4 treatment-emergent events (TEAEs) were reported in 18 of 24 (75%) dose escalation phase pts; 8 of 24 (33%) pts experienced TEAEs considered related to inobrodib; the most common being thrombocytopenia and anemia. The most frequent TEAEs (irrespective of causality) were thrombocytopenia (all grades 58.3%; [gr 3/4 37.5%] of pts) and fatigue (all grades 58.3%; [gr 3 4.2%]). Thrombocytopenia was promptly reversible when

treatment was withheld, without loss of efficacy in responders. Bleeding events were low grade (all grades 16.7%, included conjunctival hemorrhage, rectal hemorrhage, hematuria and epistaxis; [gr 3/4 0%]). Neutropenia was infrequent (12.5%, all present at baseline; [gr 3 8.2%]) and infection rate and pattern was as anticipated for the heavily pre-treated population studied (66.7%; [gr 3 37.5%, single gr 5 event]).

The main reason for discontinuation among all pts was progressive disease (18 pts, 72%) with only 2 pts (8%) discontinuing due to related events.

Following monotherapy dose escalation, a recommended phase 2 dose/schedule (RP2D) of 35mg BD, 4 days on/ 3 days off was identified. Inobrodib had a mean maximal concentration of 690 ng/ml and a half-life of 5.2 hrs which supported the selection of a BD dose.

At data cut-off (6th Feb 2023), 3/9 evaluable pts treated with inobrodib monotherapy at the RP2D had achieved objective responses (33.3%, PR 2/9 pts, VGPR 1/9 pts). Median follow-up for the RP2D cohort was 63 days (range 2-308).

The first dose escalation cohort of inobrodib in combination with the licensed dose of POM and DEX has completed. Initial data indicate the safety profile of inobrodib/POM/DEX to be similar to monotherapy with no new safety signals identified. Early efficacy data is being collected as dose escalation continues.

Summary/Conclusion:

Inobrodib is well tolerated and demonstrates promising efficacy in heavily pre-treated patients with RRMM. These results support the continued development of inobrodib in combination with standard therapies in patients with RRMM.