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POSTER ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Indolent Lymphoma: High CR and VGPR Rate with Fixed Duration Bendamustine, Rituximab and Acalabrutinib in Waldenstroms Macroglobulinaemia (BRAWM)

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Background: Waldenström's macroglobulinaemia (WM) is an uncommon lymphoproliferative disorder. Although many options are available, an optimal first-line therapy for WM has not been defined. We postulated that combining bendamustine and rituximab (BR) with a next generation BTK inhibitor would result in deeper responses as measured by complete response (CR) and very good partial response (VGPR) rates, and provide a longer duration of response.
Objectives: The primary objective of this trial is to document the CR and VGPR rates
Methods: The BRAWM clinical trial combines BR with acalabrutinib in a one-year, fixed duration treatment course including six cycles of BR and 12 months of acalabrutinib (6 months of monotherapy). This ongoing trial is taking place at 9 clinical sites across Canada and 44 patients have been enrolled as of July 1, 2023, with a recruitment goal of 59.
Results: Median age of participants was 68; 34 were male; 3 participants were low risk, 21 intermediate and 20 high risk. 27 participants completed combination therapy, 17 completed monotherapy and 7 were followed-up at 18 months, and 3 at 24 months after first dose. Table 1 shows the observed Clinical Responses using 6 th IWWM; 2 participants improved from a VGPR to a CR between cycles 7 and 12, both of whom have not reached month 18 for assessment. The interim primary endpoint of combined CR and VGPR rate is 13/17 (77%), with no participants having progressed at this interim analysis. 3 participants discontinued treatment early: 1 at cycle 7 (with a VGPR) who experienced an adverse event requiring treatment; 1 at cycle 3 with inter-current illness, and 1 at cycle 2 for personal reasons not related to treatment. The total observed Treatment Related Adverse Events (TRAEs) in combination therapy was 188 amongst 35 participants, and n= 24 in 10 participants during monotherapy. There were 24 Grade 3/4 TRAEs (combination n= 20, monotherapy n= 4). Total observed Serious Adverse Events was 18, and 7 TRSAEs 7; 6 during combination therapy (3 febrile neutropenia and 1 for each fever, allergic reaction and bowel obstruction) and 1 pneumonia during monotherapy. Grade 3/4 TRAEs resulted in 29 dose interruptions in 13 participants, and 2 dose reductions.
Mutational analysis of participants with adequate sample for assessment (n=35), showed 33 with *MYD88* mutation, 10 with a *CXCR4* mutation, and 1 with a *TP53* mutation. Minimal residual disease (MRD) analysis of Peripheral Blood (PB) and Bone Marrow, using next generation sequencing, is underway. Initial review shows that most evaluable patients (those with samples

	Screening (n=44)	Cycle 7 (n= 27) Post combination	Cycle 12 (n= 17) Post monotherapy	Month 18 (n= 7) Post therapy
Hb g/L (median)	103.5	125.5	128	126
IgM g/L (median)	38.1	1.18	0.99	1.19
CR (%)	-	0	2 (12)	0*
VGPR (%)	-	18 (67)	11 (65)	6 (86)
PR (%)	-	9 (33)	4 (23)	1 (14)
SD	-	0	0	0
PD	-	0	0	0

Figure 1

at two or more time-points) have become MRD undetectable in PB. Uni- and multi-variate analyses of variables that may be associated with outcomes is underway.

Conclusions: Bendamustine, rituximab and acalabrutinib front-line therapy for WM is safe and well tolerated and initial clinical results show that this treatment induces a high percentage of CR + VGPRs.

Table 1: Clinical Responses using 6 th IWWM. *The 2 participants observed to have a CR at month 12 have not reached month 18 for progression or survival follow-up.

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