

IWWM13

Title: Iopofosine I 131 After BTK Inhibitors in Waldenström Macroglobulinemia: CLOVER-WaM Subgroup Efficacy and Safety

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Introduction: Waldenström Macroglobulinemia (WM) remains incurable with current available therapeutic options. Treatment options for relapsed/refractory pts are limited and often continuous, underscoring the need for new agents with novel mechanisms of action and pt-centered, fixed duration therapy. Iopofosine I 131 is a novel radiopharmaceutical compound composed of a lipid raft-targeting phospholipid ether covalently bound to ¹³¹I, a beta emitting radioisotope. Here, we report preliminary sub-group results of the CLOVER-WaM study [NCT02952508] in WM pts treated with a Bruton's Tyrosine Kinase inhibitor (BTKi) immediately prior to iopofosine.

Methods: Eligible WM pts had received >2 prior therapies and had symptomatic disease requiring therapy according to consensus recommendations for WM.

Treatment consisted of 2 cycles of iopofosine I 131 administered at 15 mCi/m² on days 1 and 15 of each 57-day cycle. The primary efficacy endpoint was major response rate (MRR; partial response or better, as determined by the modified IWWM-VI). Secondary and exploratory endpoints included overall response rate (ORR), treatment-free survival (TFS), progression free survival (PFS), duration of response (DOR), and clinical benefit rate (CBR; stable disease or

better). Herein, efficacy endpoints were assessed in the modified intent-to-treat (mITT) population (all pts who received ≥ 60 mCi total administered dose of iopofosine I 131), and whose treatment regimen prior to iopofosine included a BTKi. Safety was evaluated using CTCAE v4.03 in pts who received ≥ 1 dose of iopofosine. Data cut off for this analysis was Jan. 16, 2026.

Results: As previously reported, 65 pts were dosed and 55 are included in the mITT population. Of those, 22 (40%) had received a BTKi containing regimen immediately prior to iopofosine; and 11 who previously received at least 2 regimens utilizing BTKis and 12 who were refractory to rituximab. In this subgroup, median age was 70.5 (range 55-88), 17 (77%) were male, and 5 (23%) were female. The median number of prior therapies was 3 (range 2-7), 15/22 (68%) were MYD88 mutated and 18/22 (82%) were TP53 wildtype. The MRR was 15/22 (68.2%), ORR was 19/22 (86.4%) and CBR was 100% (Figure 1), median PFS was 12 months (range 1.6 to 28.0), median DOR was 16.0 months (range 2 to 34.4) (Figure 2), and median TFS was 19.1 months (range 2.5-34.4). Grade ≥ 3 , related treatment emergent adverse events (TEAE) occurring in $> 10\%$ of pts included anemia (41%), leukopenia (41%), neutropenia (58%), and thrombocytopenia (86%).

Conclusion: Iopofosine I 131 demonstrated significant efficacy; 100% CBR, 86.4% ORR and 68.2% MRR with a median PFS of 12 months (range: 1.6 – 28.0 months) in a pt population with no current standard of care therapy. The treatment was well-tolerated with a manageable toxicity profile with cytopenias as the only Grade 3 or greater TEAE. Based on the results of this pivotal trial, iopofosine I 131 could be a promising novel treatment for WM pts after BTKi therapy.

Figure 1: Efficacy of Iopofosine I 131 ≥ 60 mCi Total Administered Dose in Immediately post-BTKi Patients (n=24)

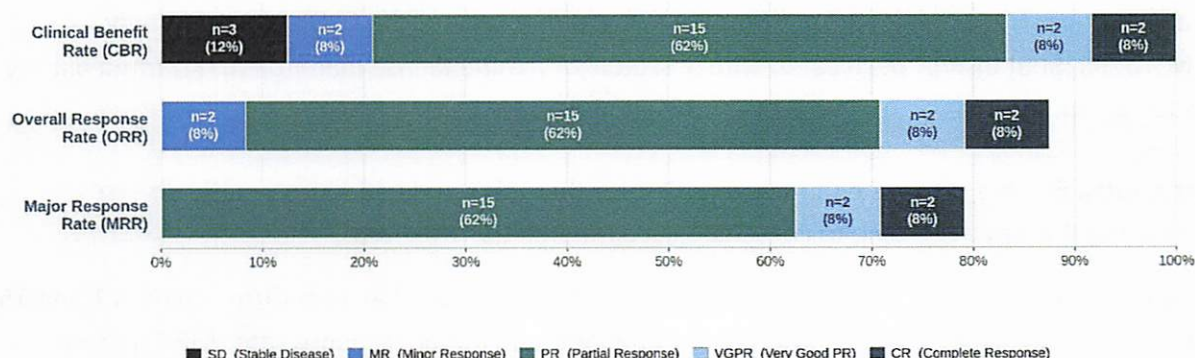
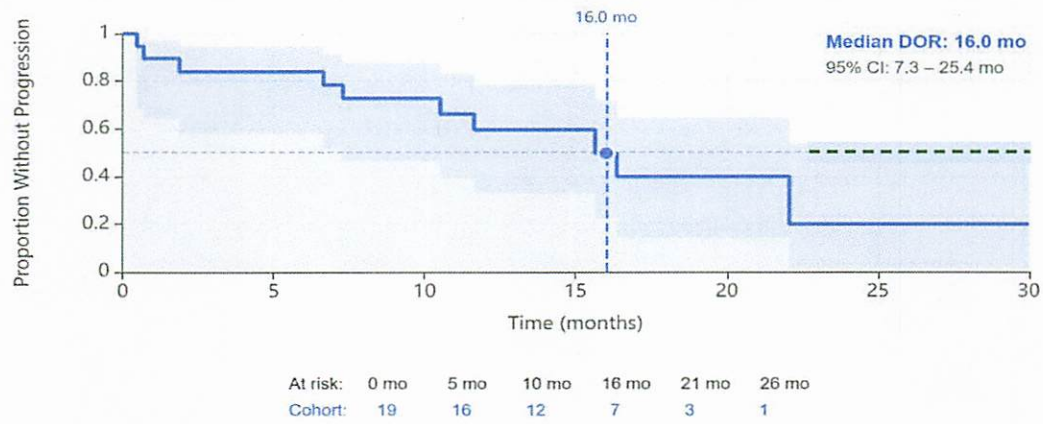


Figure 2: Duration of Response in Immediately post-BTKi Patients (n=24)



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