PHASE 2 STUDY OF IBRUTINIB WITH TEMOZOLOMIDE, ETOPOSIDE, LIPOSOMAL DOXORUBICIN, DEXAMETHASONE, RITUXIMAB (TEDDI-R) FOR SECONDARY CNS LYMPHOMA

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BACKGROUND

- Secondary CNS lymphomas (SCNSL) are aggressive, and few treatments are tolerated by patients of all ages.
- CNSLs often exhibit chronic active B-cell receptor signaling and respond to BTK inhibitors, but for short duration.
- TEDD-R + ibrutinib (TEDDI-R) achieves durable remissions in primary CNS lymphoma but has unknown activity in SCNSL.
- We present results from a response-adapted study of ibrutinib with TEDD-R in SCNSL [NCT03964090].

METHODS

- Patients with R/R or untreated SCNSL were eligible.
- Patients first received an ibrutinib window (560mg x 14d) to determine ibrutinib-responsiveness. Pts with ≥20% reduction then received TEDDI-R and pts with <20% reduction received TEDD-R, both in 4 21-day cycles along with intrathecal chemotherapy.
- CR was confirmed with FDG-PET brain/body and CSF analysis. Surveillance scans were q3m for 1y, q4m x 1y, q6m x 1y, then annually. Primary endpoint was PFS.

RESULTS

50 pts enrolled with median age 63 (range 26-89), including 16 (32%) aged ≥70. 28 (56%) had DLBCL and 16 (32%) had HGBL with *MYC* and *BCL2* or *BCL6* rearrangements. 45 (90%) were relapsed/refractory with median 2 prior therapies (range 1-4). 43 pts were evaluable for the ibrutinib window; 25 (50%) were ibrutinib-responsive and 18 (36%) ibrutinib-resistant. 86% of ibrutinib-responsive DLBCL/HGBL tumors were CD10-negative.

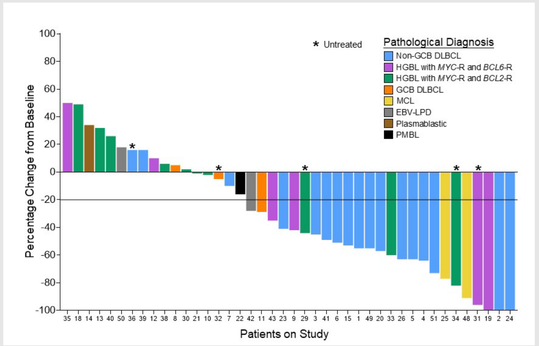


Figure 1. Response to Ibrutinib window across all histologies.

30 pts received TEDDI-R and 20 pts received TEDD-R. ORRs to TEDDI-R and TEDD-R were 93% (71% CR) and 30% (25% CR), respectively. ORR in CD10-negative DLBCL/HGBL was 75% (71% CR).

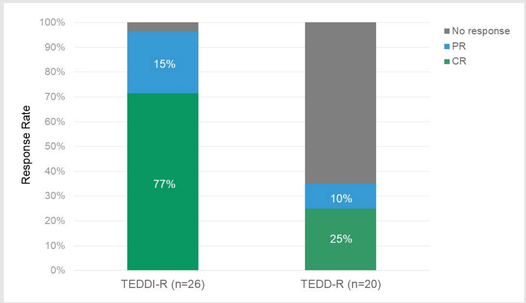


Figure 2. Response rates to TEDDI-R and TEDD-R.

Heme AEs included G3-4 (% cycles, total 138) neutropenia (40%), thrombocytopenia (12%), and anemia (37%). Febrile neutropenia occurred in 10% of cycles. G3 non-hematologic AEs included (% pts) UTI (21%), hypokalemia (21%), sepsis (15%), diarrhea (15%), hypotension (11%), adrenal insufficiency (11%), atrial fibrillation (9%). Few G4 AEs and no opportunistic infections occurred. 14 (30%) pts developed hand-foot syndrome.

After 23-month median follow-up, the 1-year PFS and OS across all pts were 37.8% and 59.9%.

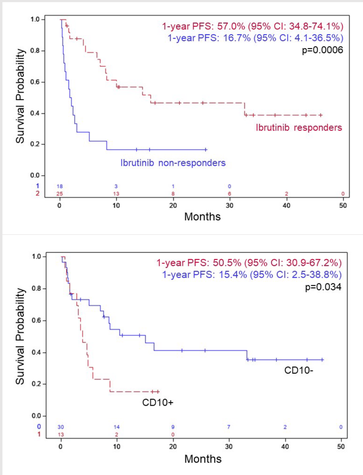


Figure 3. 1-year PFS in ibrutinib-responsive vs ibrutinib-resistant tumors (top) and CD10- vs CD10+ tumors (bottom).

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CONCLUSIONS

Ibrutinib-responsive SCNSL has a high rate of CR to TEDDI-R and remissions may be durable. Most ibrutinib-responsive tumors are CD10 negative.