BMN 673

- BMN 673 is a potent inhibitor of PARP-1 and -2.
- BMN 673 is highly effective when combined with low doses of TMZ.
- BMN 673 was tested as a single agent at 0.33 mg/kg/day x 28 days (BID x 5 d).
- Combination A: Temozolomide 30 mg/kg /d and MN673.
- Combination B: BMN 673 + TMZ combinations induced CRs that were maintained through 12 weeks and both were superior to single agent BMN 673 (5 day schedule).
- The median IC50 value for the 4 Ewing sarcoma cell lines (6.4 nM) was lower than the IC50 for the non-Ewing sarcoma cell lines (0.1 nM) (p=0.046).

BMN 673 AND TEMOZOLOMIDE (TMZ) IN VITRO

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BMN 673 SIMPLE SINGLE AGENT TESTING RESULTS:

- BMN 673 was tested as a single agent at 0.33 mg/kg/d x 28 days (BID dosing M-F and SID dosing S-S).
- BMN 673 was tested alone and with Temozolomide (TMZ).
- BMN 673 was tested as a single agent at 0.33 mg/kg/day x 28 days (BID x 5 d).
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CONCLUSIONS

- Remarkably high activity was observed for the combinations, with 5 of 10 Ewing sarcoma xenografts having CR responses maintained through at least 6 weeks for most treated animals (see figure above). Lines that did and did not meet this benchmark are listed below:
  - Progressive disease by 6 wks: ES-3, and (ES-2, ES-4, ES-5, and EW-5 not shown).
- Maintained CRs were observed both for the regimen with higher dose TMZ and the regimen with low-dose TMZ, and in general responses to the two schedules were comparable. SK-NEP-1 responded better to the low-dose TMZ regimen, while CHLA-258 responded better to the higher-dose TMZ regimen.

BMN 673 AND TEMOZOLOMIDE (TMZ) IN Vivo

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COMMENTS LIKE plot for BMN 673 against PPTP cell lines

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