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Phase 1 Pharmacokinetic and Pharmacodynamic Results of Novel Anti-Neutropenic Factor for the Prevention and Treatment of Febrile Neutropenia.

Background: Anti-Neutropenia Factor - RHO (ANF-RHO™) is a novel pegylated version of native human recombinant G-CSF protein. ANF-RHO has distinct biophysical and biological properties that produce a distinct pharmacokinetic and pharmacodynamic profile as compared pegfilgrastim (Neulasta®) that may be ideally suited for treating febrile neutropenia.

Methods: A Phase 1 clinical study was conducted in healthy volunteers to assess pharmacokinetics (PK) and pharmacodynamic (PD) profile of ANF-RHO. Subcutaneous, single dose treatment with ANF-RHO or Neulasta in ascending doses was evaluated in a randomized, controlled, double-blind study that included peripheral blood neutrophil and CD34+ analytical assessments. ANF-RHO was evaluated at doses of 5 – 50 µg/kg against both active (Neulasta) and placebo (saline) comparators. Neulasta was administered at the labeled fixed 6 mg dosage (equivalent to 80 – 100 µg/kg).

Results: ANF-RHO demonstrated a biphasic ANC response in comparison to Neulasta between days 2-7. Mean ANC counts for all ANF-RHO treated subjects showed a time to C_{max} (T_{max}) between 6.8 and 7.4 days in contrast to 2.2 days for Neulasta-treated subjects. Quantitative comparisons of ANC values showed that ANF-Rho neutrophil counts increased in a stable and prolonged manner (7 days) following treatment in contrast to Neulasta that showed a rapid ANC spike (2 days) and then decrease following administration. Assessment of AUC showed that ANF-RHO at10 µg/kg was equivalent to Neulasta at 80-100 µg/kg demonstrating a ≥8-fold potency effect over Neulasta with duration of effect lasting beyond 12 days.

Conclusion: The unique PK/PD of ANF-RHO suggests that a significantly lower dosage on the same day of chemotherapy administration to achieve neutrophil levels sufficient to mitigate severe neutropenia and with fewer dose-related side effects. The results suggest that finer control of ANC may be achieved by ANF-RHO using weight-based doing. ANF-RHO Phase 2 planning is underway with a focus on reducing or preventing the occurrence and severity of neutropenia resulting from the use of myelo-suppressive chemotherapy.

	Mean AUC	
Days Post Administration	Neulasta 100µg/kg	ANF-Rho 10µg/kg
0	3.7	2.86
2	32.6	10.1
7	15.3	16.8
12	5.2	11
%Change from 0 - 12	39	390

PD results (ANC and CD34+) were markedly prolonged in the ANF-Rho treatment groups even at the lowest dose.

Key words: Growth factor, Hematopoiesis, Myelosuppression, Neutropenia