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Treating Anemia of Cancer with Darbepoetin Alfa Administered Every 4 Weeks: Final Results from a Phase 2, Randomized, Double-Blind, Placebo-Controlled Study in Cancer Patients Not Receiving Chemotherapy and/or Radiotherapy

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Abstract

Darbepoetin alfa (DA) is an erythropoiesis-stimulating agent (ESA) approved in the USA for treating chemotherapy-induced anemia. However, cancer patients (pts) not receiving chemotherapy can still develop anemia of cancer (AoC), which is often not treated (Ludwig et al. Eur J Cancer. 2004;40:2293–2306[Medline]). As pts with AoC are not receiving chemotherapy or radiotherapy and may have few clinic visits, using an ESA with a long dosing interval, such as once monthly (Q4W), may be optimal for these pts. Results from a prior study suggested that Q4W dosing of DA is feasible since 61% of pts (n=21) with AoC receiving 6.75mcg/kg DA Q4W achieved a hematopoietic response (≥ 2 g/dL hemoglobin [Hb] rise from baseline or Hb ≥ 12 g/dL without a red blood cell transfusion in the prior 28 days) (Smith et al. Br J Cancer. 2003;88:1851–1858[Medline]). Here we report the final results of a phase 2, randomized, double-blind, placebo-controlled study of DA Q4W in pts with AoC. Pt eligibility included ≥ 18 years, non-myeloid malignancy, AoC (Hb ≤ 11 g/dL), and no chemotherapy and/or radiotherapy within 30 days of screening or during the study. Pts (n=220) were randomized 3:1 to DA (6.75mcg/kg) or placebo (PBO), with stratification based on screening Hb (<10g/dL or ≥ 10 g/dL). Pts received blinded treatment (DA or PBO) subcutaneously Q4W for 13 weeks (4 total doses); end of study was week 17. The primary endpoint was the percentage of pts with a hematopoietic response. Of the 162 DA pts, 63% were female, 73% were white, and the mean (SD) age was 70 (12) years; the 56 PBO pts had similar demographics. The Kaplan-Meier percentage (KM%) of pts with a hematopoietic response (Table) differed significantly between the DA and PBO groups (% difference [95% CL]=44% [30, 58]; $p < 0.001$). The two groups also differed significantly in the KM% of pts who achieved the target Hb of 11g/dL (% difference [95% CL]=38% [22, 54]; $p < 0.001$). Adverse events (AEs) occurred in 71% DA pts (116/164) and 72% PBO pts (39/54); the most common AE was fatigue. The incidence was 3% vs 2% for treatment-related AEs and 28% vs 28% for serious AEs in the DA and PBO groups, respectively. In 30% DA pts and 4% PBO pts, Hb reached >13g/dL. Serious thromboembolic events (deep vein thrombosis, cerebrovascular accident, and pulmonary embolism) occurred in 2.4% DA pts and in 0%

PBO pts. In summary, DA Q4W appeared to be effective and well tolerated in this study for the treatment of AoC.

Summary of Hb Results

	DA	PBO
	n=162	n=56
Hematopoietic Response		
Pts eligible for hematopoietic response analysis, n	158	54
KM% (95% CL) pts with hematopoietic response	69% (61, 77)	24% (12, 36)
Target Hb		
Pts eligible for target Hb analysis, n	139	49
KM% (95% CL) pts achieved target Hb (11g/dL)	85% (79, 92)	50% (34, 66)
Mean (SD) Hb after target achieved, g/dL	11.9 (0.8) [n=133]	11.3 (0.8) [n=28]
Change in Hb from Baseline to Week 17 (LVCF*)		
Pts eligible for analysis of change in Hb, n	158	54
Mean (SD) baseline Hb, g/dL	10.1 (0.8)	10.2 (0.8)
Mean (SD) Hb change (baseline to week 17), g/dL	1.3 (1.4)	0.2 (1.0)
*LVCF=Last value carried forward		