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Long-Term Safety Follow-up of a Randomized Trial of Darbepoetin Alpha and Intravenous Iron Following Autologous Hematopoietic Cell Transplantation

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Abstract

We recently reported the efficacy of darbepoetin alpha (DA)(Aranesp®) and intravenous (IV) iron (Venofer®) on erythroid reconstitution following autologous hematopoietic cell transplantation (auto-HCT). Although short-term disease progression, infections or other safety events were not influenced by DA or IV iron, a longer follow-up was required as some meta-analyses suggest increased mortality in patients with cancer receiving erythropoiesis-stimulating agents (ESA), particularly when no concomitant chemotherapy is administered. Besides, some in vitro and animal studies raised the possible role of iron in tumor growth. Therefore, we analyzed long-term outcome to verify the safety of DA and IV iron.

We included 127 patients with myeloma (n=76), Hodgkin's lymphoma (n=8), aggressive (n=26) or indolent (n=12) non-Hodgkin's lymphoma and other diagnoses (n=5). Groups were well balanced for age, disease, disease stage and disease status at time of transplantation. They were randomized between no erythropoietic therapy (n=25), DA from day 28 post-auto-HCT (n=52) or DA + IV iron on days 28, 42 and 56 (n=50). We collected data about infections and other complications, disease status and overall survival (OS) from auto-HCT (between March 2004 and January 2008) up to January 2014. Patients given a second transplant were censored at that time.

During long-term follow-up (mean: 3.4 years), the incidence of infection remained comparable in the 3 groups. Specifically, 3 patients in the control group (12%), 8 in the DA group (15%) and 6 in the DA+iron group (12%) experienced at least one infection. The number of infections per patient

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between day 126 (end of the study) and the last follow-up was 0.2 ± 0.7, 0.2 ± 0.4 and 0.1 ± 0.3 in control, DA and DA+iron groups, respectively (NS).

During follow-up, 4/25 (16%) patients in control group, 13/52 (25%) in DA group and 6/50 (12%) in the DA+iron group experienced at least one complications (NS). While 3 patients (2 in the control group and 1 in the DA+iron group) presented a thrombosis on study, no other thrombo-embolic event occurred during follow-up. Two patients (1 in control group and 1 in DA group) developed a benign tumor, whereas 4 patients (3 in DA group and 1 in DA+iron group) presented a secondary malignancy (NS). Other complications were: hypertension (n=2, 1 in control and 1 in DA groups), ischemic cardiomyopathy (3 in DA group) with 1 myocardial infarction, 4 arrhythmias (1 in control and 3 in DA groups) with pacemaker requirement in 2 (1 in control and 1 in DA groups), peripheral arteriopathy (1 in DA group), diabetes (n=3, 2 in DA and 1 in DA+iron groups), radiopneumonitis (1 in control group), vasculitis (1 in DA group), nephritis (1 in DA and 1 in DA+iron groups), thyroiditis (1 in DA group), spondylarthritis (1 in DA+iron group), jaw osteonecrosis in myeloma patients treated with zoledronic acid (1 in DA and 1 in DA+iron groups), hip osteonecrosis (1 in DA+iron group), peripheral neuropathy (1 in DA and 1 in DA+iron groups), sudden transient deafness (1 in DA group) and sarcoidosis (1 in DA+iron group).

We did not observe any difference in survival. Indeed, 1-year OS were 100%, 88% and 100% and 5-year OS were 86%, 78% and 91% in the control, DA and DA+iron groups, respectively (p=0.43). Progression-free survival (PFS) were also similar in the 3 groups: 1-year and 5-year PFS were 85% and 71% in the control group, compared to 86% and 57% in the DA group and 94% and 78% in the DA+iron group (p=0.30).

In conclusion, DA and IV iron therapy following auto-HCT did not affect safety, disease outcome or survival in long-term analyses.

Disclosures Beguin: *Amgen:* Consultancy, Speakers Bureau; *Vifor:* Consultancy, Speakers Bureau.

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