

# A Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial of Pegfilgrastim in Patients Receiving First-Line FOLFOX/Bevacizumab or FOLFIRI/Bevacizumab for Locally Advanced or Metastatic Colorectal Cancer: Final Results of the PAVES Study

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## Abstract

### Background

Pegfilgrastim's role in reducing febrile neutropenia (FN) risk in patients with colorectal cancer (CRC) receiving chemotherapy plus bevacizumab was not previously evaluated in a prospective study. This phase 3, double-blind trial evaluated efficacy of pegfilgrastim vs placebo in reducing grade 3/4 FN incidence in patients with advanced CRC receiving bevacizumab in combination with first-line chemotherapy (FOLFOX or FOLFIRI).

### Patients and Methods

Patients  $\geq 18$  years of age with locally advanced/metastatic CRC were randomized 1:1 to placebo or 6-mg pegfilgrastim  $\sim 24$  hours after receiving chemotherapy plus bevacizumab every 14 days. The study treatment period included 4 cycles, but patients could continue treatment for up to 60 months. The primary endpoint was grade 3/4 FN incidence in the first 4 cycles. Secondary endpoints included objective response rate (ORR), overall survival (OS), and progression-free survival (PFS) analyzed at the end of the long-term follow-up period.

### Results

A total of 845 patients were randomized between November 2009 and January 2012 (422, pegfilgrastim; 423, placebo). Pegfilgrastim significantly reduced grade 3/4 FN incidence in the first 4 treatment cycles (pegfilgrastim, 2.4% [95% CI: 1.1–4.3] vs placebo, 5.7% [95% CI: 3.7–8.3]; odds ratio [OR] 0.41;  $P=0.014$ ). No significant differences were observed between the two arms in ORR (OR 1.15,  $P=0.330$ ), and OS and PFS (hazard ratio 0.94,  $P=0.440$  and 0.93,  $P=0.300$ , respectively).

## Conclusion

Pegfilgrastim reduced FN incidence in patients with advanced CRC receiving chemotherapy and bevacizumab. Administration of pegfilgrastim was tolerable and did not negatively impact tumor response or survival in this patient population.

## Keywords:

Pegfilgrastim, colorectal cancer, febrile neutropenia, overall survival