International Society of Gastrointestinal Oncology
2013 Gastrointestinal Oncology Conference
October 17–19, 2013

TIME COURSE OF ADVERSE EVENTS IN THE VELOUR TRIAL

David R. Ferry,[1] Paul Ruff,[2] Radek Lakomy,[3] Jana Prausova,[4] Guy A. van Hazel,[5] Vladimir M. Moisyenko,[6] Raghu Vishwanath,[7] Emmanuelle Dochy,[7] Eric Van Cutsem,[8] Teresa Macarulla[9]

[1]New Cross Hospital, Wolverhampton, United Kingdom; [2]University of Witwatersrand Faculty of Health Sciences, Johannesburg, South Africa; [3]Masaryk Memorial Cancer Institute, Brno, Czech Republic; [4]University Hospital Motol, Prague, Czech Republic; [5]University of Western Australia, Nedlands, Australia; [6]LDC MIBS, St. Petersburg, Russian Federation; [7]Sanofi Oncology, Cambridge, Massachusetts, USA; [8]Leuven Cancer Institute, Leuven, Belgium; [9]Vall d´Hebron University Hospital, Barcelona, Spain

Background: The VELOUR study compared the efficacy and safety of aflibercept (ziv-aflibercept in the United States) + FOLFIRI versus placebo + FOLFIRI in 1226 metastatic colorectal cancer patients who had progressed after receiving oxaliplatin treatment. Aflibercept demonstrated statistically significant improvements in overall survival, progression-free survival, and response rate.

Methods: Within the VELOUR safety population, the time course of adverse events associated with anti-VEGF therapy as well as chemotherapy-associated adverse events were evaluated. We reviewed grade 3/4 adverse events, identified the proportion of patients with adverse events, the cycle of occurrence, and the proportion of patients with a single occurrence.

Results: The safety population was comprised of 1216 patients (aflibercept = 611; placebo = 605). Grade 3/4 adverse events occurring in more than 5% of aflibercept patients were diarrhea, neutropenia, stomatitis, infections, proteinuria, and hypertension; grade 3/4 hemorrhage occurred in only 3% of aflibercept patients. The incidence of all grade 3/4 adverse events peaked at cycle 1 or 2 and subsequently decreased with later cycles.

Conclusions: In VELOUR, many common adverse events were of single occurrence. The majority of grade 3/4 adverse events occurred during early cycles and decreased with subsequent cycles. Adverse events were generally reversible and consistent with adverse events managed by oncology clinicians. Chemotherapy-associated adverse events decreased sharply in both arms following initial event presentation. While the cause of this phenomenon is not clearly identified,

the occurrence of these events may be due to the initial use of full-dose FOLFIRI in both arms as per protocol and subsequent early dose modification.

Study was supported by Sanofi in collaboration with Regeneron Pharmaceuticals.