9209 POSTER

Safety of romiplostim for treatment of severe chemotherapy induced thrombocytopenia (CIT) in patients with lymphoma receiving multi-cycle chemotherapy: results from an open-label dose- and schedule-finding study

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Background: Current treatment options for patients with CIT are limited and are associated with potentially serious risks. The primary objective of the current study was to identify a safe dose and schedule of romiplostim, a peptibody that increases platelet (PLT) production, in lymphoma patients receiving multi-cycle chemotherapy.
Methods: Eligible lymphoma patients experienced grade 3 or 4 thrombocytopenia (PLT count $<50\times10^9$/L) during a prestudy chemotherapy cycle. Patients received the same chemotherapy regimen (CHOP, ICE, or ESHAP with or without rituximab) during the first treatment cycle as during the previous qualifying cycle. A single subcutaneous injection of romiplostim (100, 300, 700, or 1000 μg) was administered 1 day after completing chemotherapy.
Results: Patient characteristics and safety and efficacy results are given in the Table. ECOG status was higher, and baseline PLT counts were lower, in the 700 and 1000 μg romiplostim groups. Use of specific chemotherapy regimens was not balanced between treatment groups. Adverse events (AEs) were consistent with those expected in lymphoma patients receiving multi-cycle chemotherapy. There was no dose-dependent effect of adding romiplostim to chemotherapy on the incidence of AEs or serious AEs when differences in baseline characteristics were accounted for. One patient with stage IV gastric lymphoma died (700 μg group) following a serious AE of gastrointestinal hemorrhage that was considered possibly related to romiplostim by the investigator. There was no evidence of a beneficial effect of romiplostim on the change in PLT nadir or other secondary efficacy endpoints.
Conclusions: Adding romiplostim to multi-cycle chemotherapy appeared tolerable in lymphoma patients with CIT. Further studies are warranted to explore different romiplostim doses and schedules including potential predosing before chemotherapy and multiple day dosing per cycle.

	Romiplostim				
	100 μg (N = 8)	300 μg (N = 11)	700 μg (N = 11)	1000 μg (N = 9)	Total (N = 39)
ECOG⩾1, n (%)	3 (38)	3 (27)	9 (82)	7 (78)	22 (56)
Baseline PLT $\times10^9$/L, mean (SD)	317 (162)	294 (208)	231 (79)	206 (78)	258 (142)
AEs, n (%)	6 (75)	9 (82)	8 (73)	9 (100)	32 (82)
Treatment-related AEs, n(%)	0	1 (9)	3 (27)	4 (44)	8 (21)
Serious AEs, n (%)	0	1 (9)	3 (27)	3 (33)	7 (18)
Serious treatment-related AEs, n(%)	0	0	1 (9)	0	1 (3)
PLT nadir change[A] $\times10^9$/L, median (range)	15 (−18, 55)	9 (−10, 61)	−4[B] (−16, 45)	−11 (−29, 48)	1 (−29, 61)

[A]From qualifying cycle to first romiplostim treatment cycle; [B]One patient in the 700μg group did not complete the first treatment cycle and was not included in efficacy analyses

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Bendamustine vs. fludarabine as second-line treatment in chronic lymphocytic leukemia

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Background: Bendamustine (B) demonstrated clinical activity in a wide range of pretreated hematological and non-hematological malignancies due to its unique mechanism of action distinct from classical alkylating agents reducing cross-resistance.
Material and Methods: Patients (pts) with relapsed CLL requiring treatment after one previous systemic regimen (usually chlorambucil-based, not including fludarabine (F) or B) were randomized centrally to either receive B 100 mg/m^2 as a 30-minute-infusion on days 1 + 2 of a 4week (w) cycle, or the "standard treatment" consisting of F 25 mg/m^2 on days 1 to 5 q 4w. Treatment was repeated until diagnosis of best response or up to a maximum of 8 cycles. The primary objective was to achieve comparable progression-free survival (PFS) to F in the treatment arm with B.
Results: Out of a total of 96 pts randomized between 2001 and 2006, 92 were eligible for the analysis, 49 allocated to B and 43 to F. B/F median age: 68/69 years, male pts: 63% in both arms, Binet C stage: 55/49%, B symptoms:41/38%, respectively. Bulky disease (11/14%) was equally distributed, while a favourable performance status was more frequent in the B group (43/29%). First-line treatment consisted of chlorambucil or the Knospe regimen in 96% of pts. About half of the pts received six or more cycles in either treatment arm. Overall response rates (ORR) were 78% (B) and 65% (F), clinical CR rates 29/10%. After a median follow-up of approximately three years and 79 events recorded, median PFS was 20.0/15.6 months (hazard ratio 0.87; 90% confidence interval: 0.59−1.28, p = 0.27). 24/26 pts have died after a median of 44/41 months (hazard ratio 0.82; 90% confidence interval: 0.51−1.30, p = 0.48). Hematotoxicity was marginally more frequent in the B arm, while non-hematological toxicities were generally rare, with B/F grade 3/4 infections of 13/15%, respectively. Conclusions: These data suggest at least comparable efficacy of B to F with respect to ORR, PFS and overall survival, pointing to an alternative treatment option to F in relapsing CLL pts after chlorambucil containing first line chemotherapy.

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Dose dense R-CHOP-14 may be superior to conventional R-CHOP-21 with comparable toxicities in Asian patients with high risk Diffuse Large B Cell Lymphoma

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Background: Although the addition of Rituximab, to standard cyclophosphamide, doxorubicin, vincristine and prednisolone given every 21 days (R CHOP-21) significantly improves outcomes of patients with diffuse large B cell lymphoma (DLBCL) compared to CHOP-21 alone, about 40% of patients will relapse. Studies suggest that shortening the interval between chemotherapy cycles from 21 to 14 days increase dose intensity and may improve outcomes. This approach is not widely adopted, particularly in Asia, because of the impression that Asians tolerate dose-dense chemotherapy poorly. Further, the benefit of R-CHOP given every 14 days (R-CHOP-14) over R-CHOP-21 has not been demonstrated. This study aims to compare the safety and efficacy of R-CHOP-14 with R-CHOP-21.
Methods: Two hundred seventy five patients with DLBCL treated with curative intent from 2003 to 2008 were included: 52 received R-CHOP-14; 223 received R-CHOP-21.
Results: About 40% in each group had high risk disease, defined as the presence ⩾3 high risk factors (age > 60, high LDH, poor performance status, advanced stage and ⩾2 extranodal sites). After median follow up of 23 months, event free survival (EFS) was 87% and 73% for R-CHOP-14 and R-CHOP-21 respectively (HR 0.65, 95% CI: 0.8−1.5 p = 0.32). The overall survival (OS) was 93% and 79% for R-CHOP-14 and R-CHOP-21 respectively (HR 0.5, 95% CI: 0.15−1.6 p = 0.25). Among patients with high risk disease, R-CHOP 14 resulted in improvement in EFS (HR 0.24 95% CI: 0.08−0.085 p = 0.03). There is also significant improvement in OS (HR 0.13 95% CI: 0.02−0.96 p = 0.05). Toxicity profiles were similar in both arms; no treatment related mortality was reported. Therapy was delivered on time for dose-dense treatment arm in 88% of cycles.
Conclusion: This is the first report on R-CHOP-14 in Asians. R-CHOP-14 is safe and may confer an advantage in patients with high risk disease and should be evaluated in this group of patients, a study we are currently embarking.

9212 POSTER

Rituximab does not seem to influence the risk of central nervous system occurrence in patients with diffuse large B cell lymphoma

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Background: The introduction of Rituximab into the therapy of Diffuse Large B Cell Lymphoma (DLBCL) dramatically improved the prognosis.