410 POSTER

Platinum (II) complexes with phosphine-ferrocene containing ligands and their *in vitro* activity against leukemia

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Purpose: Platinum-amino complexes, *e.g.*, cisplatin, carboplatin (paraplatin), oxaliplatin, *etc.* were known to have anti-tumour activity against certain types of tumour cell lines. In this study, a new class of heterobimetallic platinum-iron complexes with mixed phosphine and sulphur containing ligands were synthesized and screened against leukemia cell line P_{388}.

Methods: The complexes *cis*-[Pt{(Ferr)$_2$PhP}(DMSO)X_2], where X_2 = Cl_2, C_2O_4, $O_2(CO)_2(C_6H_{11})_2$ and $O_2(CO)_2C\text{-}CH_2CH_2$ have been synthesized and characterized physicochemically and spectroscopically. These complexes were tested *in vitro* against leukemia cell line P_{388} using the MTT-assay, and compared with those for both cisplatin, carboplatin, oxaliplatin & 5-fluorouracil (5-FU).

Results: Two of these complexes showed significant cytotoxic activity against P_{388} cells which possess one order of magnitude better activity than cisplatin & 5-FU and two and three orders of magnitude better activity than carboplatin & oxaliplatin.

Conclusion: The present results are encouraging since these complexes are novel and represent new analogues to cisplatin & carboplatin, however, further *in vitro* tests are required using other cell lines like the human breast (T_{47D}) & the non-small-cell lung (A_{549}) to confirm the above results before any *in vivo* tests.

411 POSTER

Prospective analysis of factors affecting CD34+ cells mobilization in breast cancer patients

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Purpose: To analyze clinical (age, stage, regimens and cycles of prior chemotherapy (CT), interval from the last CT, radiotherapy) and biological (% and count of CD34+ cells/mL in steady-state bone marrow (BM) and blood) factors influencing CD34+ cell mobilization in breast cancer pts.

Methods: One hundred and two pts with breast cancer received 3 different mobilization programmes: 24 pts Cyclophosphamide (Cy) 4 g/m^2 or FEC (Fluorouracil 600 mg/m^2, Epirubicin 75 mg/m^2 and Cy 600 mg/m^2) + G-CSF 5 μg/Kg/d s.c. from d + 1 (G5) and 78 pts G-CSF 10 μg/Kg/d s.c. alone (G10). Daily leukapheresis (LK) were started when CD34+ cells/mL count in blood was >2500. The objective was a minimum collection of 2 x 10^6 CD34+ cells/Kg.

Results: Median age was 42 yrs (26–59). Median number of prior CT cycles 6 (3–14). Median days from the last CT until mobilization 30 (18–147). Median blood and BM steady-state CD34+ cell % were 0.012% (0–0.2) and 0.9% (0.1–6), respectively. Median BM CD34+ cell count was 3.3 x 10^5/mL (0.1–44.1). A high correlation was observed between preLK CD34+ blood cell count and CD34+ cells collected (r = 0.78; p = 0.000). A median of 2 (1–7) LK per pt was performed.

	Max. peak	CD34+/Kg/m	%CD34+ in bag	Failures
CT + G5	113300 ± 9571	648 ± 503	1.6 ± 1.36	0/24 (0%)
G10	66547 ± 58492	279 ± 170	0.66 ± 0.31	3/78 (4%)
	p = 0.0084	p = 0.000	p = 0.000	n.s.

Number of previous chemotherapy cycles had an inverse correlation with both maximum peak of CD34+ cells and CD34+ cells collected (r = −0.22, p = 0.023 and r = −0.23, p = 0.022 respectively).

	BM CD34+/mL		Prior cycles:	
	< percentil 25	> 25	<5	>5
Peak CD34 (x 10^5/mL)	3.6 ± 2	9.1 ± 8.7 *(p = 0.0056)*	15 ± 16.2	6.7 ± 4.7 *(p = 0.002)*
CD34+ (kg/mL)	317 ± 414	389 ± 301 *(p = 0.37)*	637 ± 496	326 ± 272 *(p = 0.001)*

Correlation analysis of maximum blood CD34+ cells/mL with BM CD34+ cells/mL was significantly positive (r = 0.35, p = 0.001). Prior CT cycles had an inverse correlation with BM CD34+ cells/mL (r = −0.15, p = 0.145) and differences between ≤5 and 6 or more previous chemotherapy cycles was significant (p = 0.031).

Conclusions: CT+G5 mobilizes better than G10 and provides a purer cell yield that might facilitate a further cell manipulation. Extensive prior CT might decrease CD34+ cells in BM and compromise mobilization results.

412 POSTER

Idarubicin in advanced or relapsed multiple myeloma treatment in elderly

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Idarubicin (IDA) is on analogue of doxorubicin with elevate cytotoxic activity. Bone marrow toxicity is dose-limiting; the drug is claimed to be less toxic than doxorubicin. It is active when given by mouth because of its lipophilia. We report our experience about IDA treatment of relapsed or progressive Multiple Myeloma (M.M.) in elderly. We studied 18 patients (10 M – 8 F, aged 67–80 years) with M.M. st. II–III (12 A – 6 B) and M component: Ig G-k = 8; Ig A-k = 4; Ig G-λ = 2; Ig A-λ = 1; B.J. = 3. All pts. were previously treated with melphalan + prednisone; 10 pts. in maintenance with α- IFN. Our schedule was the following: IDA 10 mg/m2 + PDN 80 mg/m2 4/28 days for 6 cycles, os, at home

Exclusion's criteria were: age <65 years; st. I; heart and renal failure; diabetes. We obtained good response on 16/18 pts. with seric M.C. of 50% and urinary of 65% decrease (respectively range 20–70% and 50–80%). Two non responder pts. were Ig A M.M. Performance status was 0 on 7 and I on 9 pts; neutropenia was II on 9, III on 8, IV on 1 pt.; nausea on 2 and alopecia on 3 pts.

Conclusions: IDA + PDN association is good effective and tolerated, with excellent control of advanced M.M. in elderly, prolonged survival, quality life improvement and easy treatment schedule.

413 POSTER

Incidence of delayed infections after high-dose chemotherapy with peripheral blood stem cell support

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High-dose chemotherapy (HD-CHT) with autologous bone marrow rescue (ABMR) induces profound and persistent immune disturbances. In the period following neutrophil recovery, opportunistic infections associated to cellular and antibody-mediated immune deficiency have been reported in a significant number of pts treated with ABMR. Reinfusion of peripheral blood stem cells (PBSCs) after HD-CHT induces faster neutrophil and platelet recovery than ABMR. We have studied the incidence of infections after neutrophil recovery in pts treated with HD-CHT+PBSCs and whether incidence correlated with the number of CD34+ PBSCs reinfused. Fifty-three of 59 pts with solid tumors or lymphoma treated with HD-CHT + PBSCs at a single institution (1995–1996) survived after neutrophil recovery. Nine (16.9%) had late infections (operatively defined as infections presenting after neutrophil recovery). Late infections appeared in 3 of 10 pts (30%) with non-Hodgkin's lymphoma, 3 of 33 pts with breast cancer (9%) and 3 of 16 pts with other malignancies (18%). Type of infection: interstitial pneumonitis (5 pts), superficial candidiasis + fever (2 pts), herpes zoster (1 pt), *Mycobacterium avium* infection (1 pt). Median time from PBSC infusion to infection was 26 days (range 6–210). One pt with interstitial pneumonitis died. All others recovered after a median period of 7 (0–21) days on antimicrobial agents and 7 days (0–21) in hospital. The median number of CD34+ cells reinfused (x 10^6/Kg) was 2.9 (1–5.7) in 9 pts who had late infections vs. 4 (1.9–16.5) in 41 pts who did not develop late infections (p < 0.05). Infections presenting after neutrophil recovery cause substantial mobility in pts treated with HD-CHT+PBSCs. The number of CD34+ cells reinfused is inversely correlated with the risk of late infections.

414 POSTER

Use of the delta assay of plastic adherent progenitors (PD) to measure early haemopoietic precursors in peripheral blood harvests

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Purpose: To determine the relationship between plastic adherent early stem cell progenitors and engraftment following peripheral blood progenitor cell (PBPC) rescue.

Methods: 30 patients (pts) undergoing high dose chemotherapy and PBPC rescue were studied for relationship of harvest CD34+ cell count, granulocyte-macrophage colony forming units (CFU-GM) and plastic adher-