(grade 1). Grade 2 toxicities included hyperglycemia (n = 4) and diarrhea (n = 1). There were no relationships between specific toxicity and dose level, and no detectable differences in the incidence or severity of adverse events between the first cycle and subsequent cycles. Partial responses were obtained in nine patients and stable disease in three that required a second line of chemotherapy (taxanes-based regimen) and all patients developed a skin rash during this chemotherapy (without concomitantly administration of nimotuzumab). No antibodies to nimotuzumab were detected. The optimal biological dose has not reached yet. Further dose escalation and analysis of pharmacodynamic is ongoing.
Conclusions: Nimotuzumab administered concomitantly with chemotherapy was safety and well tolerated. No severe adverse reactions were detected and the antibody showed a low immunogenecity. Skin rash was observed for first time after using nimotuzumab in combination with doxorrubicin and cyclophosphamide. The maximum tolerated dose and the optimal biological dose have not reached yet.

733 POSTER

The administration of pegfilgrastim following myeloablative chemotherapy for sufficient peripheral blood stem cell (PBSC) mobilization in patients with solid organ tumors and lymphomas

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Background: The classical methods of peripheral blood progenitor cell mobilization consist of daily administration of filgrastim following myeloablative chemotherapy. New forms of G-CSF with prolonged half life time reduce patients' stress, improve their compliance and possibly contribute to improvement of PBSC mobilization. The aim of the study was to investigate whether sufficient harvesting of cells is achieved with pegfilgrastim as well as to determine the optimal dose.
Materials and Methods: Two groups of patients with solid tumors and lymphomas received either 6 mg or 12 mg of pegfilgrastim, 24 hours following the administration of high dose chemotherapy (cyclophosphamide 4.5 g/m^2 or etoposide 1.2 g/m^2). Daily blood samples for CD34+ cells were obtained after peripheral blood leucocyte recovery following leucocytopenia due to chemotherapy.
Results: Twenty three patients were included in the study and the parameters studied are listed in the table. No statistically significant difference was observed between the two groups for these parameters (p = ns).

Groups	Patient number	Apheresis day, median value (range)	MNC$\times 10^8$/kg, median value (range)	CD34$\times 10^6$/kg, median value (range)	WBC$\times 10^3$/l median value (range)
Group 1 (pegfilgrastim 6 mg)	14	13 (7–18)	2.405 (1.06–6.61)	4.91 (1.22–16.17)	7.2 (4.2–13.4)
Group 2 (pegfilgrastim 12 mg)	9	10 (7–13)	3.91 (1.77–6.45)	5.88 (3.64–34.15)	8.5 (5.4–18.1)

Conclusion: The number of the harvested PBSC's following myeloablative chemotherapy is sufficient after 6mg of pegfilgrastim and comparable to that collected following daily filgrastim, as previously described by our group.

Immunotherapy

Poster presentations (Thu, 27 Sep, 08:00–11:00) Immunotherapy

800 POSTER

MOR202 – a fully human antibody targeting CD38 for the treatment of multiple myeloma and other forms of blood-borne malignancies

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CD38 is a cell surface protein expressed by a variety of hematopoetic cells. Overexpression of CD38 seems to play a key role in various forms of leukaemia and – even more pronounced – in multiple myeloma (MM). To date, MM is an incurable malignancy with a median survival period of three to four years after diagnosis.
Fully human antibodies directed against CD38 were selected by cell panning strategies from the MorphoSys HuCAL GOLD® phage display library. The lead candidate MOR202 was chosen from several antibodies recognizing different epitopes on CD38.
MOR202 was subject to comprehensive in vitro- and in vivo-studies: It displays a low nanomolar affinity to CD38 and recognizes the protein on a wide variety of cancer cell lines as well as on all primary MM patient samples tested in FACS and IHC analysis. In the human IgG1 format, MOR202 is able to kill CD38-positive cell lines and primary MM cells from patients by antibody-dependent cell-mediated cytotoxicity (ADCC) with picomolar EC_{50} values, whereas progenitor cells remain unaffected as shown by a clonogenic assay. Furthermore, MOR202 reduces tumour growth (RPMI8226) in a SCID-mouse model and increases the animals' overall survival rate. The excellent efficacy in the SCID xenograft model was even superior to the effects of Velcade® tested in the same study.
In summary, MOR202 appears to be a promising candidate for the treatment of MM and other CD38-related diseases.

801 POSTER

A strategy for generation of human tumor-specific T cell lines for adoptive transfer in follicular lymphoma patients

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Background: Adoptive T-cell therapy using donor lymphocyte infusions is a promising approach for treating hematological malignancies. But, efficacy is limited by the induction of graft-versus-host disease. Transfer of tumor-specific T-cell lines or clones could enhance the graft-versus-tumor effect and eliminate graft-versus-host disease. However, isolating antigen-specific T-cell lines is a time-consuming and laborious process. We tried to optimize expansion of tumor-specific autologous T-cell lines from patients with follicular lymphoma.
Materials and Methods: Lymphoma-specific T-cell lines were generated by repeated in vitro stimulation of lymphocytes isolated from tumor or blood with autologous soluble CD40 ligand-activated tumor cells. On day −3, tumor cells were obtained from frozen lymphoma sample by CD3 depletion and activated with sCD40L + IL-4 for 72 hours. On day 0, TILs obtained from frozen lymphoma sample by CD19 depletion or CD3 enriched autologous PBMCs were cocultured with activated tumor cells at the ratio of T cell 1 vs. tumor cells 4. Cytokines (IL2 and IL15) were supplemented 48 hrs after starting culture. T cells were harvested on day 10 and restimulated with tumor cells. A total of 4 rounds of stimulations were done. To determine whether the presence or absence of immunostimulatory or immunosuppressive factors in the tumor microenvironment influence the generation and function of lymphoma-specific T cells, the surface expression of co-stimulatory/co-inhibitory molecules (CD40, CD54, CD58, CD80, CD86, PDL1, PDL2, B7H3, B7H4, BTLA, ICOS-L) expression before and after tumor activation with sCD40L + IL-4 was evaluated.
Results: Autologous tumor-reactive T-cell lines were generated in 8/11 follicular lymphoma patients. Two T-cell lines & clones were reactive against native autologous FL cells (Group A). Six T-cell lines & clones didn't show reactivity against native autologous FL cells, but were reactive against sCD40L activated autologous FL cells (Group B). Three T-cell lines & clones did not recognize native or activated tumor cells (Group C). Expression of most co-stimulatory molecules on the tumor cells was comparable between the three different groups before and after activation with sCD40L. But, ICOS-L expression was low in 2/3 patients in whom tumor-reactive T-cell lines could not be generated (Group C).
Conclusions: Tumor-specific T-cell lines could be generated by co-culture with autologous soluble CD40 ligand-activated tumor cells and confirmed to retain specificity against autologous tumor cells in a cytokine induction assay. This approach could be successfully used to isolate lymphoma-specific T-cell lines from follicular lymphoma patients.