



56th ASH® Annual Meeting and Exposition

San Francisco, CA • December 6-9, 2014

ABSTRACTS & PROGRAM



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-Author name in bold denotes the presenting author

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 denotes an abstract that is clinically relevant.

 denotes that this is a recommended PHD Trainee Session.

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Last updated November 21, 2014. Please note that this site represents the latest program changes and differs from the print version in some details.

2440 Vaccination with a New Generation of Fast Dendritic Cells Transfected with mRNA from hTERT, Survivin and Autologous Tumor Mount Strong Immune Responses and Prolong Survival

Program: Oral and Poster Abstracts

Session: 703. Adoptive Immunotherapy: Poster II

Sunday, December 7, 2014, 6:00 PM-8:00 PM

North Building, Hall E (Moscone Center)

Iris Bigalke, MD^{1*}, **Kirsti Honnashagen^{2*}**, **Marianne Lundby^{2*}**, **Julitta Kasten^{3*}**, **Else Marit Suso Inderberg, PhD^{2*}**, **Lisbeth Skoge^{2*}**, **Stein Saboe-Larssen, PhD^{2*}**, **Dolores J Schendel, PhD^{4*}** and **Gunnar Kvalheim, MD, PhD¹**

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We have previously shown in preclinical models that a new generation of fast dendritic cells (DCs), using a maturation cocktail containing IL-1 β , TNF α , IFN γ , PGE2 and the TLR7/8 ligand R848, is more efficient than the standard 7 day DCs matured with a cytokine cocktail as described by Jonuleit (standard DCs). These DCs show a high up-regulation of HLA-DR and co-stimulatory molecules like CD80, CD83, CD86 and CD40 combined with a down regulation of CD14. They have a good migratory capacity towards CCL19 and their special characteristic is IL-12p70 production when stimulated with CD40L whilst IL-10 production is low.

We investigated if the new generation DCs maintain their properties when produced by GMP standards and if they are able to mount specific immune responses in patients. Monocytes were enriched using the Elutra cell separator and cultivated either fresh or after cryopreservation. Monocytes were cultured in Teflon bags in the presence of IL-4 and GM-CSF and the maturation cocktail was added on day 2 or 3. After 24 hours DCs were harvested and electroporated with mRNA. After 2-4 hours recovery, cells were frozen with either 2.5E+6 or 5E+6 transfected DCs per vial. DC productions from one lung cancer, one prostate cancer, four glioblastoma and one AML patient showed the same characteristics with only some variations in the amounts of IL-12p70 released after co-culture with CD40L transfected mouse fibroblasts.

The first patient treated with the new generation DCs transfected with hTERT and survivin mRNA suffered from stage IV lung cancer with brain metastases. Following diagnosis in June 2011 she was treated with chemotherapy and radiotherapy. Since December 2011 she has been vaccinated and has obtained a status of stable disease. DC vaccination was interrupted in 2/2013 when an attempt was made to re-open an occluded bronchus with radiotherapy. During irradiation the patient developed an inflammation of the pleura, which was treated with high dose cortisone. While on cortisone therapy the patient developed 2 new brain metastases, which were treated with local radiotherapy using the Cyberknife. DC vaccination was continued in 6/2013 and health conditions gradually improved bringing the patient again into a stable disease with no further development of brain metastasis.

The second patient receiving DC vaccination had a hormone resistant prostate cancer in a very advanced stage and dropped out immediately after start of treatment.

Additionally, four stage IV glioblastoma patients have been treated with hTERT and survivin transfected DCs plus either with autologous tumor mRNA or, where no tumor RNA was available, with hCMVpp65 mRNA DCs. The observation time of these four patients is currently 14, 11, 11 and 10 months and all patients remained in complete remission. All patients treated with the new generation DCs show strong local DTH responses and flu-like symptoms after vaccination at a significantly earlier time point than previously observed by us in patients treated with standard DCs.

Altogether our results show that the new generation DCs can successfully be produced from patients with different kinds of cancer. Clinical results, strong DTH reactions and flu like symptoms following DC vaccinations suggest that

specific immune responses have occurred. To further confirm these observations immune monitoring of individual patients is under investigation and results from these studies will be presented.

Disclosures: **Schendel:** *Medigene:* Employment, Equity Ownership, Patents & Royalties.

See more of: [703. Adoptive Immunotherapy: Poster II](#)

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