

# World Congress on **Breast Cancer**

August 03-05, 2015 Birmingham, UK

## **Radio-immunotherapy of cancer: Therapeutic efficacy, underlying mechanisms and potential applications**

**Inge Verbrugge**

The Netherlands Cancer Institute, Netherlands

**R**adiotherapy is one of the most successful cancer therapies but may benefit from coincident or subsequent immunotherapy. We designed novel combinations of radiotherapy with immunomodulatory monoclonal antibodies (mAbs) that were evaluated in pre-clinical mouse breast cancer models. We demonstrate that in combination with both single-dose and fractionated radiotherapy, mAbs designed to enhance T-cell function [anti-( $\alpha$ )-CD137] and relieve immunosuppression through blocking T-cell inhibitory signaling [ $\alpha$ -programmed death (PD)-1] induce tumor regression in up to 100% of mice. Radio-immunotherapy induced immunological memory in cured mice and CD8<sup>+</sup> T-cells were critical for its therapeutic efficacy.

Radiotherapy up regulates MHC class I (MHCI) expression on tumor cells, which may further support immune-mediated killing. We show that this involves mTOR activation by ionizing radiation by a still unresolved mechanism. Yet, mTOR is important as mTOR inhibition almost completely abrogated the therapeutic effect of radio-immunotherapy. We conclude that radio-immunotherapy effectively cures mice that bear established mammary tumors and that therapy response is critically dependent on the activity of cytotoxic T-lymphocytes as well as on mTOR signaling. We predict that other tumor types to which T-cells are present in the peripheral repertoire and in which radiotherapy is used as a primary course of treatment, will also respond to radio-immunotherapy.

### **Biography**

Inge Verbrugge is an Associate Staff Scientist, at The Netherlands Cancer Institute in Amsterdam. Her primary research interest is in understanding and exploiting potential synergy between localized radiotherapy and immune-modulatory antibodies ('radio-immunotherapy') in cancer treatment. She received her PhD from the University of Amsterdam in 2009 and was subsequently awarded two prestigious Fellowships (Dutch Cancer Society Post-Doctoral fellowship and 'Bas Mulder Award') to study the anti-cancer potential of radio-immunotherapy. This work was initiated at the Peter MacCallum Cancer Centre in Melbourne, Australia and continued at the Netherlands Cancer Institute. She published 14 papers as first or second author in reputed journals.

### **Notes:**