Contribution ID: **47**   Type: **Invited**

Preclinical development with Nanobodies with a focus on ovarian cancer

Wednesday, 1 May 2019 09:30 (30 minutes)

Approximately, 10-30% of ovarian cancers have an amplification of the human epidermal growth factor receptor type 2 (HER2) gene or overexpression of its protein product, while it is present at low levels in normal tissues. HER2 is a 185 kDa transmembrane protein that belongs to the HER family of tyrosine kinase receptors. Although controversial, recent studies have confirmed that HER2 overexpression in ovarian cancer is associated with worse patient outcome, implicating HER2 may be a potential prognostic biomarker for ovarian cancer patients.

With the aim of diagnostic imaging of HER2, specifically targeting anti-HER2 Nanobodies have been developed and preclinically validated in SKOV-3 ovarian cancer mouse models. Nanobodies are camelid derived single-domain antibody fragments that are ten times smaller than classic antibodies. These vector molecules reach their in vivo target very rapidly while unbound Nanobody is cleared from the body. This allows for fast high contrast imaging compared to imaging with monoclonal antibodies. This also implicates that short-lived radionuclides such as 68Ga, 18F and 99mTc can be used for radiolabeling. The 68Ga-anti HER2 Nanobody has been succesfully translated to a Phase I clinical trial in breast cancer patients.

Alternatively, the anti-HER2 Nanobody has been fluorescently labeled with the near-infrared IRDye800CW to use as a tool for real-time visualization of tumor lesions during fluorescence-guided surgery. As debulking surgery is still the most effective treatment for advanced ovarian cancer, the efficiency of surgery is of utmost importance. Significantly reduced residual tumor was observed with Nanobody image guidance as compared to conventional surgery.

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Session Classification: Ovarian cancer (PARTII)

Track Classification: Preclinical research and development of new radiopharmaceuticals