reovirus as a pre-conditioning regimen performed significantly better than the simultaneous or preceding administration of bsAbs. This combination treatment also induced regressions of non-injected distant lesions, suggesting that this therapy might be effective for metastatic disease.

Conclusions Oncolytic reovirus administration represents an effective strategy to induce a local IFN response and strong T cell influx, thereby sensitizing the tumor microenvironment for subsequent CD3-bsAb therapy (figure 1). Our data advocate for the inclusion of oncolytic viruses as a pre-conditioning strategy in T cell engaging antibody trials for solid tumors. Since both CD3-bispecific antibodies and oncolytic viruses are in advanced clinical development as monotherapies, efficient translation of this combination seems feasible.

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Ethics Approval All mouse studies were approved by the institutional Animal Welfare Body of Leiden University Medical Center and carried out under project licenses AVD116002187004 or AVD116002153271, issued by the competent authority on animal experiments in the Netherlands (named CCD).

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591 COMPARISON OF TWO OHSV VECTORS FOR THE TREATMENT OF GliobLASTOMA

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Background Glioblastoma multiforme (GBM) is the most common human brain cancer. Despite a well-established standard of care, the 5-year mortality rate of GBM patients is 95%, highlighting the need for innovative therapeutic interventions. A variety of oncolytic viruses, including those derived from herpes simplex virus (oHSV), have been designed for GBM therapy, but early-phase clinical trials have reported few complete responses and no evidence of durable anti-tumor immunity. Potential reasons for the lack of efficacy are limited vector potency (i.e., virulence) and the presence of a highly immunosuppressive tumor microenvironment (TME) comprised of few vital immune cell composition. However, the presence of vital MDSCs, natural killer cells, CD8+ or CD4+ T-cells, and TME immune cell composition. However, the presence of vital adaptive immune cell types within the TME was not observed at 2 days post oHSV treatment.

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592 ENHANCING THE THERAPEUTIC POTENTIAL OF ONCOlyTIC ADENOVIRUSES WITH VSENS Technology

Goo-Young Kim*, Ji Yeon Son, So Jin Lee, Sang Wook Jo, Changhoon In, Sang Hoon Kim, Joon Young Park, So-Young Kim, Gun Young Moon, Ji-Hye Choi, Suk Hwan Kim, Minhyuk Yun, Hye Yeong Nam, Helen Cho. Samyang Biopharmaceuticals Corporation, Gyeonggi-do, Korea, Republic of

Background Oncolytic viro-therapeutics is a promising treatment for cancer. Among the different strains of oncolytic viruses currently being developed, potent cytolytic activity, manageable safety profiles, large genomic capacity for addition of transgenes and available advanced manufacture processes make adenovirus (Ad) a great choice. However, the delivery of Ad for clinical application is limited due to 1) neutralization by pre-existing neutralizing antibodies (nAb) in bloodstream and 2) receptor restricted tumor-cellular entry. To overcome these limitations, we developed a novel proprietary

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Background Oncolytic viro-therapeutics is a promising treatment for cancer. Among the different strains of oncolytic viruses currently being developed, potent cytolytic activity, manageable safety profiles, large genomic capacity for addition of transgenes and available advanced manufacture processes make adenovirus (Ad) a great choice. However, the delivery of Ad for clinical application is limited due to 1) neutralization by pre-existing neutralizing antibodies (nAb) in bloodstream and 2) receptor restricted tumor-cellular entry. To overcome these limitations, we developed a novel proprietary
polymer nanoparticle delivery system, so called Stabilized Enhanced Nano Shells (SENS™) for the delivery of Virus (vSENS).

**Methods** SENS™ employs proprietary an ionizable cationic lipid and biodegradable and biocompatible polymers. Following complexation with replication-incompetent adenovirus serotype 5 (Ad-vSENS) or replication-competent oncolytic adenovirus serotype 5 (OAd-vSENS), the physicochemical properties of the complexes were characterized by dynamic light scattering (DLS) and electron microscopy. The benefit of vSENS in coxsackievirus and adenovirus receptor (CAR) restricted cellular transduction of adenovirus was evaluated with Ad-vSENS in CAR negative cancer cells. Pharmacokinetic profile of OAd-vSENS was examined in mice following systemic administration to assess the protective effect of vSENS in the presence of pre-existing immunity to Adenoviral proteins. Anti-tumor efficacy was evaluated in syngeneic subcutaneous tumor mice models. The serum level of alanine aminotransferase (ALT) in mice was evaluated by blood chemistry analyzer.

**Results** Ad-vSENS effectively infected cancer cells in CAR-independent manner, where cancer cell-killing effects of OAd-vSENS were significantly enhanced in CAR negative cancer cells compare with those of naked OAd. When vSENS is complexed with an adenovirus, it encapsulates the virus like a shell shielding the adenovirus. Consistently, in syngeneic tumor bearing mice with pre-existing Ad immunity, longer virus blood half-life and longer survival of the mice were observed when administered with OAd-vSENS compared to naked OAd. The hepatotoxicity of OAd was greatly reduced by vSENS formulation as evidenced by the absence of acute spike in serum ALT levels typically seen after systemic administration of OAd.

**Conclusions** The results show the potential of vSENS as a novel platform technology for delivery of Ad to overcome challenges adenovirotherapies face in the clinic. vSENS platform is expected to expand the efficacy of the virus from cancer patients with high CAR expression to patients with limited CAR expression often associated as the cancer progresses. The platform is likely to facilitate treatment in patients with high levels of antibodies to adenovirus by shielding the virus from neutralization and increasing the bioavailability.

**Ethics Approval** The study was approved by Samyang Biopharmaceuticals Institution’s Ethics Board, approval number SYAU2009.

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**TUMORAL MELANOSIS MIMICKING RESIDUAL MELANOMA AFTER T-VEC TREATMENT**

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**Background** Talmogene laherparepvec (T-VEC) has become an increasingly popular treatment option for surgically non-resectable, recurrent melanoma based on its durable efficacy and safety profile. The complete response (CR) rate has been reported to be ~20% with a median of ~9 months to achieve it. Assessment of treatment response in those studies has predominantly relied on the clinical impression of the size and color of the lesions. However, in the real-world, decrease of tumor size often occurs rapidly within the first 2–3 months, while improvement of the pigmentation takes several more months. Such clinical observation of lasting pigmentation could be explained by tumoral melanosis – a histopathologic term referring to the presence of a melanophage-rich inflammatory infiltrate without remaining viable tumor cells.

**Methods** We hypothesized that residual pigmentation of stable melanoma lesions while on successful T-VEC treatment may represent tumoral melanosis. We also report practical information of such phenomenon including timeline and clinical features.

**Results** We report 6 cases of metastatic cutaneous melanoma treated with T-VEC with excellent pathologic responses. Biopsies of 5 cases were performed after observing variable clinical changes in the injected tumors, with some shrinking or becoming flat, while others grew or became raised. The range of time to biopsy was 4–23 months from the initial treatment date. Pathologic evaluation macular lesions demonstrated non-viable tumor tissue with tumoral melanosis in all cases. In an additional case, clinically increased size of the injected tumor prompted surgical excision, which similarly showed tumoral melanosis without viable tumor. Of note, while size of the tumor was increased, SUV max of the lesion decreased from prior assessment on PET-CT. No patient has developed regrowth or recurrent melanoma of the injected lesions to date (table 1).

**Conclusions** In patients receiving T-VEC treatment, pathologic CR may be achieved within the first 2–3 months, which precedes clinical improvement of pigmentation. To decrease unnecessary additional T-VEC treatment and assess the response correctly, serial biopsy of stable pigmented lesions should be considered to assess for the presence or absence of viable tumor.

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