Vimseltinib is a Selective CSF1R Inhibitor for TGCT

Smith et al. | Page 2098

Colony stimulating factor 1 receptor (CSF1R)-dependent cells in the microenvironment (such as macrophages and osteoclasts) contribute to angiogenesis, tumor growth, metastasis, and bone degradation. In this First Disclosure, Smith and colleagues present the characterization of vimseltinib, a selective oral inhibitor of CSF1R in tenosynovial giant cell tumor (TGCT). Vimseltinib depleted macrophages and CSF1R-dependent cells and inhibited tumor growth in preclinical studies. Clinically, the authors present three patients whose CSF1R biomarkers and tumor burden were reduced. Their data supports the continued clinical development of vimseltinib for TGCT.

QBS10072S Treats Breast Cancer Brain Metastasis

Deng et al. | Page 2110

The triple-negative subtype of breast cancer (TNBC) carries the highest rate of parenchymal brain metastasis (BrM) and leptomeningeal metastasis (LM). In this manuscript, Deng and colleagues disclose the nitrogen mustard-based compound QBS10072S. QBS10072S delayed tumor growth and reduced leptomeningeal dissemination in a preclinical brain metastasis model. Interestingly, the compound was able to target micro-metastases, which remains a difficult aspect of detecting and treating LM. As the compound was well-tolerated, the continued development of QBS10072S for TNBC LM patients is warranted.

ATR Inhibitor Enhances NSCLC Brain Metastasis Radiotherapy

Baschnagel et al. | Page 2129

Brain metastases occur in approximately 30% of NSCLC patients, leading to significantly worse prognosis. Stereotactic radiotherapy and/or whole brain radiotherapy is currently standard of care for these patients. To increase the effectiveness of radiation therapy in NSCLC brain metastases, Baschnagel and colleagues administered the ATP-competitive ATR inhibitor M6620. M6620 radiosensitized patient-derived xenografts in mice by inhibiting pChk1 and reducing DNA double-strand break (DSB) repair. Ultimately, this resulted in longer overall survival in the preclinical model. Their results support the ongoing phase I clinical study of M6620 in combination with whole brain irradiation (NCT02589522).

Antagonistic CD73 Antibody

Wurm et al. | Page 2250

Adenosine acts as an immunosuppressor by suppressing T cells and dendritic cells and stimulating regulatory T cells. Adenosine is generated in the tumor microenvironment by CD73 from AMP released by cell turnover. In this study, Wurm and colleagues generate a humanized antagonistic CD73 antibody, mAb19. Combining mAb19 with PD-1 inhibition increased T cell activation in vitro. They also demonstrate the combination of mAb19 with the adenosine receptor agonist ADORA3 and doxorubicin, which is known to increase adenosine levels. mAb19 therefore inhibits immunosuppression from the adenosine pathway and is suited for continued development as a cotherapy with immune-targeted or chemotherapy.

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