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IN BRIEF

FROM AACR—BREAST CANCER

Have Faith in the PALOMA-1 trial

At the plenary session of the AACR, the phase II PALOMA-1 trial results were presented in which the cyclin-dependent kinase 4/6 inhibitor, palbociclib, was combined with letrozole and compared with letrozole alone in the front-line setting for the treatment of women with metastatic disease. The trial consisted of two parts: in part one, 66 post-menopausal women with ER-positive, HER2-negative breast cancer were enrolled and in part two, 99 patients were additionally screened for *CCND1* amplification, the loss of *p16*, or both. There was a significant improvement in median progression-free survival for women treated with the palbociclib combination (20.2 months) compared with letrozole alone (10.2 months). These treatment effects were retained when both parts of the trial were assessed separately.

Original article Finn, R. S. *et al*. Final results of a randomized phase II study of PD0332991, a cyclin-dependent kinase (CDK)-4/6 inhibitor, in combination with letrozole vs letrozole alone for first-line treatment of ER+/HER2- advanced breast cancer (PALOMA-1; TRIO-18) [abstract]. *Proc. Ann. Meeting AACR* CT101 (2014).

FROM AACR—IMMUNOTHERAPY

PD-1 targeting: correlating marker expression and outcome

The relationship between PD-L1 expression and activity of anti-PD-1 antibodies is unclear. Now, in a phase I clinical trial of MK-3475—a humanized monoclonal IgG4 antibody against PD-1—tumour expression levels of PD-L1 were shown to correlate with tumour response and progression-free survival (PFS) in 135 patients with melanoma treated with the agent. The median PFS was 36 weeks and the 6-month overall survival rate was 89%. In a separate study of 38 patients with non-small-cell lung cancer (NSCLC), the median PFS was 9 weeks, and 24% of patients had a response according to immune-related response criteria. These preliminary results indicate that PD-L1 is an important biomarker for patients with melanoma and NSCLC treated with MK-3475.

Original article Daud, A. I. *et al*. Antitumor activity of the anti-PD-1 monoclonal antibody MK-3475 in melanoma(MEL): correlation of tumor PD-L1 expression with outcome [abstract]. *Proc. Ann. Meeting AACR* CT104 (2014) | Gandhi, L. *et al*. MK-3475 (anti-PD-1 monoclonal antibody) for non-small cell lung cancer (NSCLC): antitumor activity and association with tumor PD-L1 expression [abstract]. *Proc. Ann. Meeting AACR* CT105 (2014).

FROM AACR—HAEMATOLOGICAL CANCER

AG-221, first-in-class IDH2 mutation inhibitor shows promise

Cancer metabolism represents an important emerging field regarding novel tumour targeting. Mutations in the isocitrate dehydrogenase 2 (IDH2) enzyme confer a novel gain-of-function in cancer cells that results in the accumulation and secretion of a metabolite that alters cell differentiation. In an ongoing phase I trial of AG-221—a first-in-class inhibitor of mutated IDH2—in patients with relapsed or refractory acute myeloid leukaemia or myelodysplastic syndrome, the drug was shown to be well tolerated with no dose-limiting toxic effects and good clinical activity, even at the lowest dose tested. So far, 7 out of 10 patients have had a complete remission, indicating IDH2 is a promising therapeutic target.

Original article Stein, E. *et al*. Clinical safety and activity in a phase I trial of AG-221, a first in class, potent inhibitor of the IDH2-mutant protein, in patients with IDH2 mutant positive advanced hematologic malignancies [abstract]. *Proc. Ann. Meeting AACR* CT103 (2014).