MEDICAL MEDIA RELEASE

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FOR IMMEDIATE USE

Australia's novel dual immunotherapy set to be reimbursed for unresectable or metastatic melanoma

(AUSTRALIA, Melbourne, Sunday, January 21, 2024) – OPDUALAG™ (nivolumab/relatlimab) – Australia's first combined anti-PD-1/anti-LAG-3 treatment for adult and paediatric patients aged 12 years or older with unresectable or metastatic melanoma – will be listed on the Pharmaceutical Benefits Scheme (PBS), effective February 1, 2024.[1]

OPDUALAG is a fixed-dose combination of nivolumab, a programmed cell death protein 1 (PD-1) inhibitor, and relatlimab, a novel first-in-class lymphocyte-activation gene 3 (LAG-3)-blocking antibody,[1] which restores the effector function of exhausted T-cells and promotes antitumour activity.[1-3]

The PBS reimbursement of OPDUALAG (nivolumab/relatlimab) was supported by clinical trial data from Phase 2/3 RELATIVITY-047 study in patients with treatment naïve unresectable Stage III or metastatic melanoma. At a median follow-up of 13.2 months, nivolumab/relatlimab more than doubled the median progression-free survival (PFS) compared to nivolumab alone at 10.1 months vs 4.6 months, respectively (hazard ratio [HR] 0.75 [95% CI 0.62-0.92], p=0.006).[3] The safety profile of nivolumab/relatlimab combination was consistent with the profile of nivolumab. There were no new safety signals with longer medium follow-up of 25.3 months, with Grade 3 or 4 treatment-related adverse events occurring in 22% of patients in the nivolumab/relatlimab group, and in 12% of patients in the nivolumab group.[3-4]

According to Co-Medical Director of Melanoma Institute Australia, and 2024 NSW Australian of the Year, Professor Georgina Long, AO, Sydney, despite significant progress in the treatment of patients with metastatic melanoma over the past decade, more needs to be done to help improve outcomes.

"Over the past decade, the use of drugs that inhibit immune checkpoints has changed how unresectable or metastatic melanoma is treated, making long-term survival a real possibility for patients.[5] However, more needs to be done to increase the number of patients who survive.

"Inhibiting LAG-3 with relatlimab, in combination with nivolumab, gives us a new treatment to add to our toolkit against melanoma.

"Today's approval is particularly significant, as it shows commitment and focus on bringing innovative drug therapy options to patients, and targeting two different immune checkpoints — LAG-3 and PD-1 – does just that," said Professor Long

Founder and Director of the Melanoma & Skin Cancer Advocacy Network (**MSCAN**), Tamara Dawson, Melbourne, similarly welcomed the reimbursement of OPDUALAG for Australians aged 12 years and over living with unresectable or metastatic melanoma.

"While great progress has been made in the treatment of advanced melanoma, we need more treatment options that are affordable.

"Australians living with advanced melanoma and their families therefore welcome the PBS listing of a new combination immunotherapy treatment on the PBS," Ms Dawson said.

Medical Director for Bristol-Myers Squibb Australia and New Zealand, Dr Melinda Munns, Melbourne, echoed Ms Dawson's sentiments, stating the reimbursement of OPDUALAG represents another step toward improving affordable treatment access for Australians living with the potentially devastating disease.

"While we have made great progress in the treatment of advanced melanoma over the past decade, Bristol-Myers Squibb is committed to expanding dual immunotherapy treatment options for this patient group.

"The RELATIVITY-047 study demonstrated the important benefit of inhibiting both LAG-3 and PD-L1 with our novel immunotherapy combination," said Dr Munns.

About RELATIVITY-047

RELATIVITY-047 is an international, multi-centre, randomised, double-blinded Phase 2/3 clinical trial that evaluated the safety and efficacy of a fixed dose combination of nivolumab and relatlimab in patients with previously untreated or metastatic melanoma compared to nivolumab monotherapy.[3]

A total of 714 patients were randomised 1:1 to receive OPDUALAG (nivolumab 480mg/relatlimab 160mg) or nivolumab (480mg), administered in a single intravenous infusion every four weeks.[3] The study population had a median age of 63 years, was 41.7% female, and excluded patients with active autoimmune disease, medical conditions requiring systemic treatment with moderate or high dose corticosteroids or immunosuppressive medications, history of myocarditis, uveal melanoma, and active or untreated brain or leptomeningeal metastases.[3,5]

RELATIVITY-047 met its primary endpoint of progression-free survival (PFS), more than doubling the median progression-free survival (PFS) with nivolumab/relatlimab compared to nivolumab monotherapy (10.1 months vs 4.6 months, respectively; HR 0.75 [95% CI 0.62-0.92], p=0.006).[3] The 12-month PFS was 47.7% with OPDUALAG compared with 36.0% with nivolumab alone (p-value not evaluated).[3] The secondary endpoint of overall survival (OS) was not significant, with the median OS not reached with nivolumab/relatlimab versus 34.1 months with nivolumab monotherapy (HR 0.80; 95% CI, 0.64 to 1.01; p=0.059).[6] The safety profile of nivolumab/relatlimab combination was consistent with the profile of nivolumab, with no new safety signals with the combination therapy versus nivolumab alone.[3-4] The incidence of Grade 3/4 treatment-related adverse events was 22% of patients in the nivolumab/

relatlimab group and in 12% of patients in the nivolumab group.[3-4] The most common (≥1%) Grade 3/4 adverse events seen with nivolumab/relatlimab included musculoskeletal pain, hepatitis, adrenal insufficiency, diarrhoea, fatigue, rash, nephritis/renal dysfunction, and laboratory blood test abnormalities.[1,3] Treatment-related adverse events led to discontinuation in 14% of patients treated with nivolumab/relatlimab and 6% of patients receiving nivolumab.[3]

About OPDUALAG

OPDUALAG is a fixed-dose combination of nivolumab, a PD-1 inhibitor, and relatlimab, a novel first-in-class LAG-3-blocking antibody.[1] LAG-3 and PD-1 are immune checkpoints that negatively regulate T-cell proliferation and effector function.[1,3] In metastatic melanoma, LAG-3 and PD-1 are often over- and co-expressed in immune cells, contributing to T-cell exhaustion that can reduce tumour-fighting function.[1,2] The inhibition of these two immune checkpoints by OPDUALAG, therefore, supports T cell function and is the mechanism of action behind OPDUALAG's anti-tumour activity.[1-3]

OPDUALAG is indicated for the treatment of patients with unresectable or metastatic melanoma who are at least 12 years old.[1]

Further information about OPDUALAG can be found in the Product Information here.

Disclosure

Bristol Myers Squibb supports disclosure and transparency on interactions between the healthcare industry and healthcare professionals, to ensure public trust and confidence. No expert spokespeople have been offered compensation for their involvement in this media campaign. All expert spokespeople have been briefed on the approved use of this product and their obligations, with regard to promotion to the general public.

About Bristol Myers Squibb™

Bristol Myers Squibb™ is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol Myers Squibb™, visit us at BMS.com/au or follow us on LinkedIn, Twitter, YouTube, Facebook and Instagram.

Bristol Myers Squibb: Creating a Better Future for People with Cancer

Bristol Myers Squibb is inspired by a single vision — transforming patients' lives through science. The goal of the company's cancer research is to deliver medicines that offer each patient a better, healthier life, and to make cure a possibility. Building on a legacy across a broad range of cancers that have changed survival expectations for many, Bristol Myers Squibb researchers are exploring new frontiers in personalized medicine and, through innovative digital platforms, are turning data into insights that sharpen their focus. Deep understanding of causal human biology, cutting-edge capabilities and differentiated research platforms uniquely position the company to approach cancer from every angle.

Cancer can have a relentless grasp on many parts of a patient's life, and Bristol Myers Squibb is committed to taking actions to address all aspects of care, from diagnosis to survivorship. As a leader in cancer care, Bristol Myers Squibb is working to empower all people with cancer to have a better future.

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AUSTRALIAN PRODUCT INFORMATION:
https://rss.medsinfo.com.au/bq/pi.cfm?product=bqpopdu

PBS INFORMATION: Authority required. Refer to PBS Schedule for full authority information.
Before prescribing, please refer to the approved OPDUALAG™ product information (available at https://rss.medsinfo.com.au/bq/pi.cfm?product=bqpopdu). The Product Information is also available upon request from BMS Medical Information Department: 1800 067 567.

Before prescribing, please review the full Product Information and black triangle for OPDUALAG (click HERE).

References

1 Therapeutic Goods Administration. Australian Product Information for OPDUALAG™ (nivolumab/relatlimab) (2023).
2 Woo, S.-R. *et al*. Immune Inhibitory Molecules LAG-3 and PD-1 Synergistically Regulate T-cell Function to Promote Tumoral Immune EscapeLAG-3 and PD-1 Synergistically Prevent Antitumor Immunity. *Cancer research* 72, 917-927 (2012).
3 Tawbi, H. A. *et al*. Relatlimab and Nivolumab versus Nivolumab in Untreated Advanced Melanoma. *New England Journal of Medicine* 386, 24-34, doi:10.1056/NEJMoa2109970 (2022).
4 Tawbi et al. Nivolumab (NIVO) plus relatlimab (RELA) vs NIVO in previously untreated metastatic or unresectable melanoma: 2-year results from RELATIVITY-047. Oral presentation at ASCO 2023 Annual Meeting. Presentation 9502. 2–6 June, Chicago, IL, USA.
5 Tawbi, H. A. *et al*. Relatlimab and Nivolumab versus Nivolumab in Untreated Advanced Melanoma, Supplementary Appendix. *New England Journal of Medicine* 386, 24-34, doi:10.1056/NEJMoa2109970 (2022).
6 Long, G. V. *et al*. Overall Survival and Response with Nivolumab and Relatlimab. *NEJM Evid* 2(4), doi: 10.1056/EVIDoa2200239 (2023).