Opdualag®
(nivolumab/relatlimab)

Mode of Action

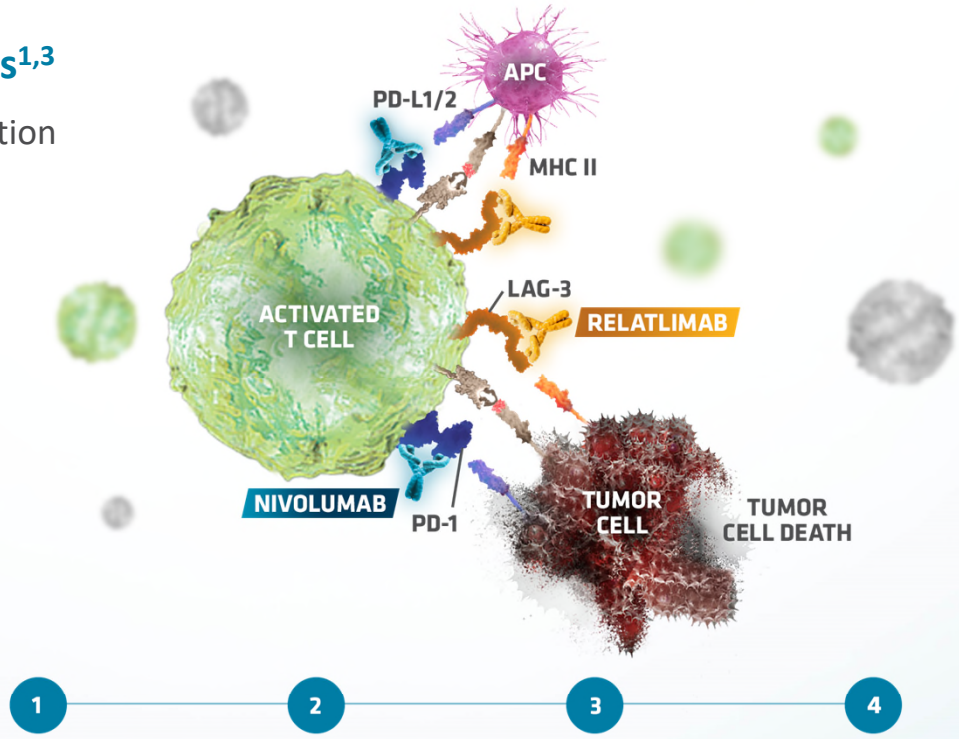
1425-BE-2400008 02/2024

Bristol Myers Squibb™

OPDUALAG® SYNERGISTICALLY ACTS ON LAG-3 AND PD-1 TO INCREASE T-CELL ACTIVITY AND COUNTER T-CELL EXHAUSTION[1,2,3]

LAG-3 and PD-1 are two distinct immune checkpoints[1,3]

- Relatlimab binds to the LAG-3 receptor and blocks its interaction with the ligands, including MHC II, reducing LAG-3 pathway-mediated inhibition of the immune response, thereby promoting T-cell proliferation and cytokine secretion[1]
- Nivolumab binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, thereby relieving T-cell exhaustion and improving cytokine production[1]
- The combination of nivolumab- and relatlimab-mediated inhibition increases T-cell activity compared to the activity of either antibody alone[1]

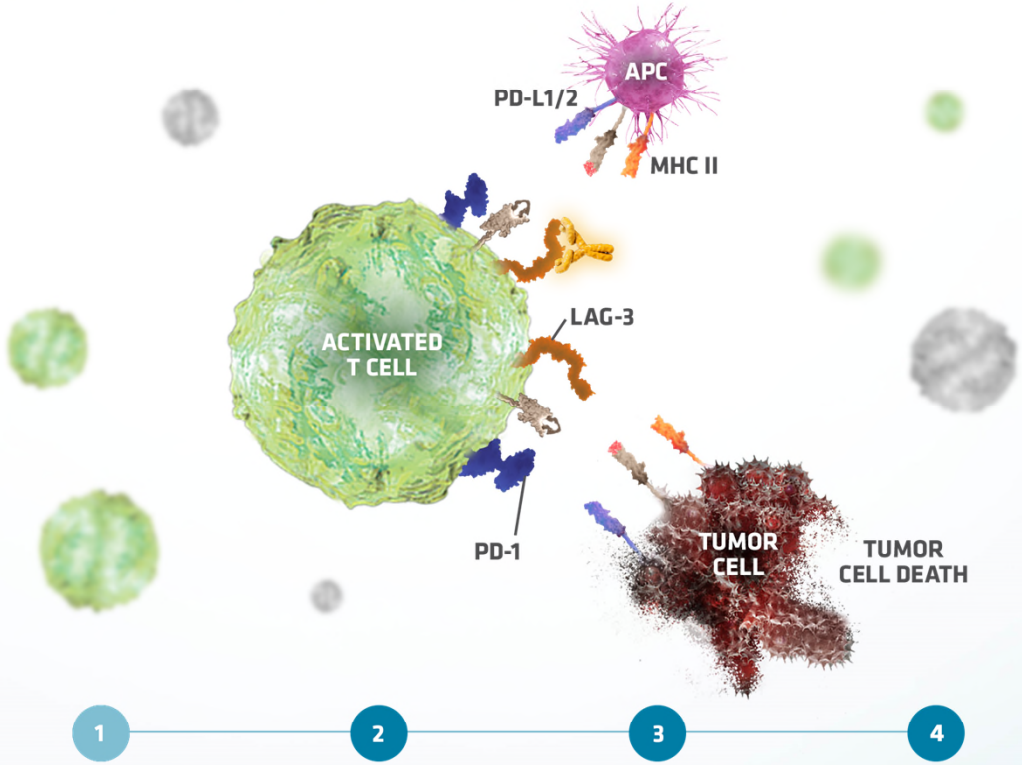


Targeting of normal cells can occur.
The illustrated mechanism of action may vary for each patient and may not directly correlate with clinical significance
APC, antigen-presenting cell; **LAG-3,** lymphocyte-activation gene 3; **MHC II,** major histocompatibility complex II; **PD-1,** programmed death receptor-1; **PD-L1,** programmed death ligand 1; **PD-L2,** programmed death ligand 2

1. SmPC Opdualag®. 2. Long L, Zhang X, Chen F, et al. The promising immune checkpoint LAG-3: from tumor microenvironment to cancer immunotherapy. *Genes Cancer*. 2018;9(5-6):176-189. 3. Tawbi HA, Schadendorf D, Lipson EJ, et al. Relatlimab and nivolumab versus nivolumab in untreated advanced melanoma. *N Engl J Med*. 2022;386(1):24-34

OPDUALAG® SYNERGISTICALLY ACTS ON LAG-3 AND PD-1 TO INCREASE T-CELL ACTIVITY AND COUNTER T-CELL EXHAUSTION[1,2,3]

- LAG-3 is a cell-surface molecule expressed on T cells and other immune cells [2,3,4]

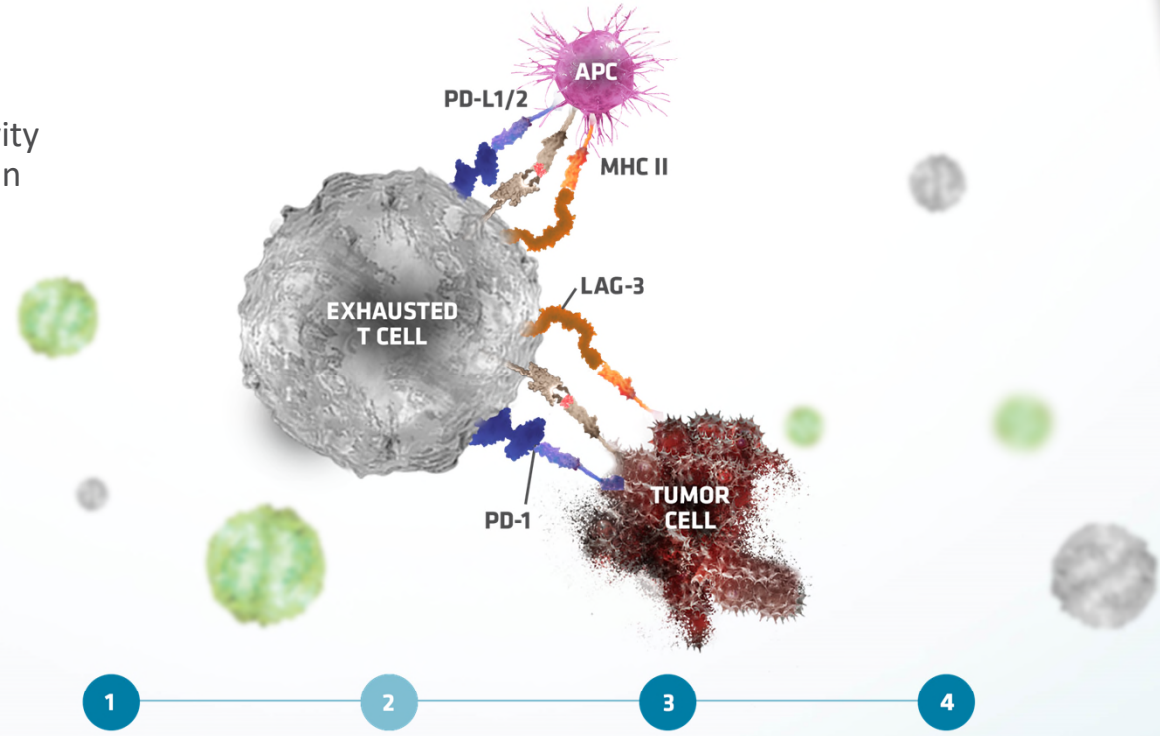


Targeting of normal cells can occur.
The illustrated mechanism of action may vary for each patient and may not directly correlate with clinical significance
APC, antigen-presenting cell; **LAG-3,** lymphocyte-activation gene 3; **MHC II,** major histocompatibility complex II; **PD-1,** programmed death receptor-1; **PD-L1,** programmed death ligand 1; **PD-L2,** programmed death ligand 2

1. SmPC Opdualag®. 2. Long L, Zhang X, Chen F, et al. The promising immune checkpoint LAG-3: from tumor microenvironment to cancer immunotherapy. *Genes Cancer*. 2018;9(5-6):176-189. 3. Tawbi HA, Schadendorf D, Lipson EJ, et al. Relatlimab and nivolumab versus nivolumab in untreated advanced melanoma. *N Engl J Med*. 2022;386(1):24-34. 4. Grosso JF, Kelleher CC, Harris TJ, et al. LAG-3 regulates CD8+ T cell accumulation and effector function in murine self- and tumor-tolerance systems. *J Clin Invest*. 2007;117(11):3383-3392

OPDUALAG® SYNERGISTICALLY ACTS ON LAG-3 AND PD-1 TO INCREASE T-CELL ACTIVITY AND COUNTER T-CELL EXHAUSTION[1,2,3]

- Activation of the LAG-3 pathway triggers inhibitory activity that reduces the function of effector T cells, leading to an impaired ability to attack tumor cells and an increased potential for tumor growth[2,3]
- LAG-3 and PD-1 are two distinct inhibitory immune checkpoint pathways that act synergistically on effector T cells, leading to the inhibition of T-cell proliferation and impaired cytokine production[1,3,4]

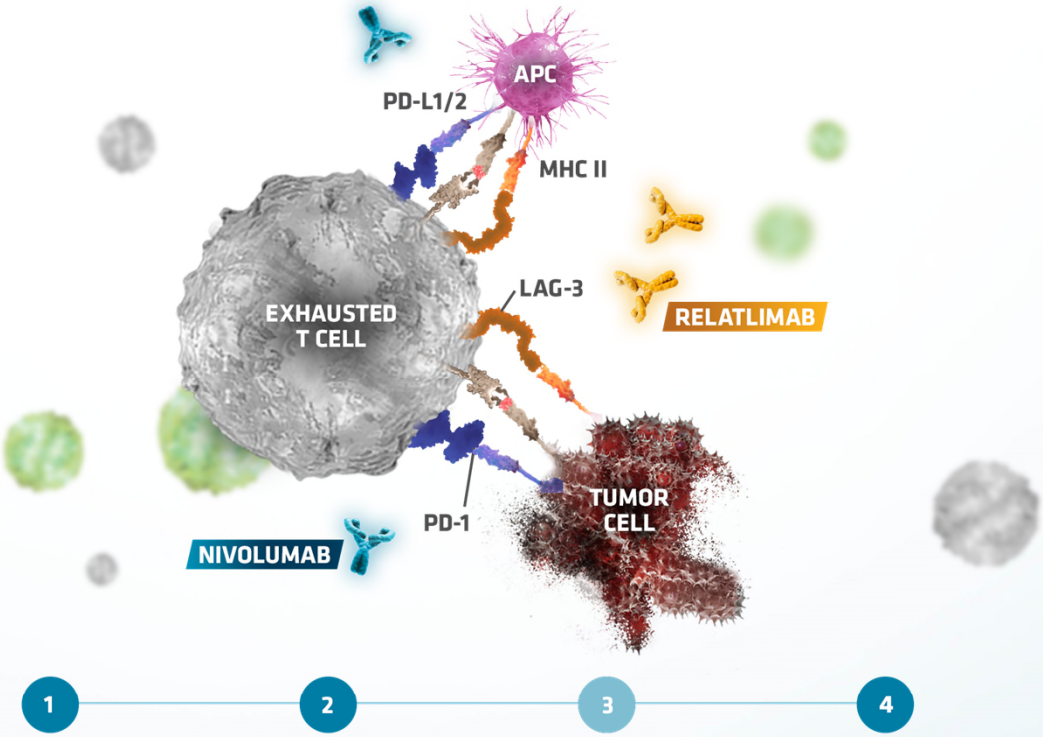


Targeting of normal cells can occur.
The illustrated mechanism of action may vary for each patient and may not directly correlate with clinical significance
APC, antigen-presenting cell; **LAG-3,** lymphocyte-activation gene 3; **MHC II,** major histocompatibility complex II; **PD-1,** programmed death receptor-1; **PD-L1,** programmed death ligand 1; **PD-L2,** programmed death ligand 2

1. SmPC Opdualag®. 2. Long L, Zhang X, Chen F, et al. The promising immune checkpoint LAG-3: from tumor microenvironment to cancer immunotherapy. *Genes Cancer*. 2018;9(5-6):176-189. 3.Tawbi HA, Schadendorf D, Lipson EJ, et al. Relatlimab and nivolumab versus nivolumab in untreated advanced melanoma. *N Engl J Med*. 2022;386(1):24-34. 4. Woo S-R, Turnis ME, Goldberg MV, et al. Immune inhibitory molecules LAG-3 and PD-1 synergistically regulate T-cell function to promote tumoral immune escape. *Cancer Res*. 2012;72(4):917-927

OPDUALAG® SYNERGISTICALLY ACTS ON LAG-3 AND PD-1 TO INCREASE T-CELL ACTIVITY AND COUNTER T-CELL EXHAUSTION[1,2,3]

- Combined nivolumab (anti-PD-1) and relatlimab (anti-LAG-3) inhibition results in increased T-cell activation compared to the activity of either antibody alone. This leads to an initiation of an improved antitumor immune response[1]

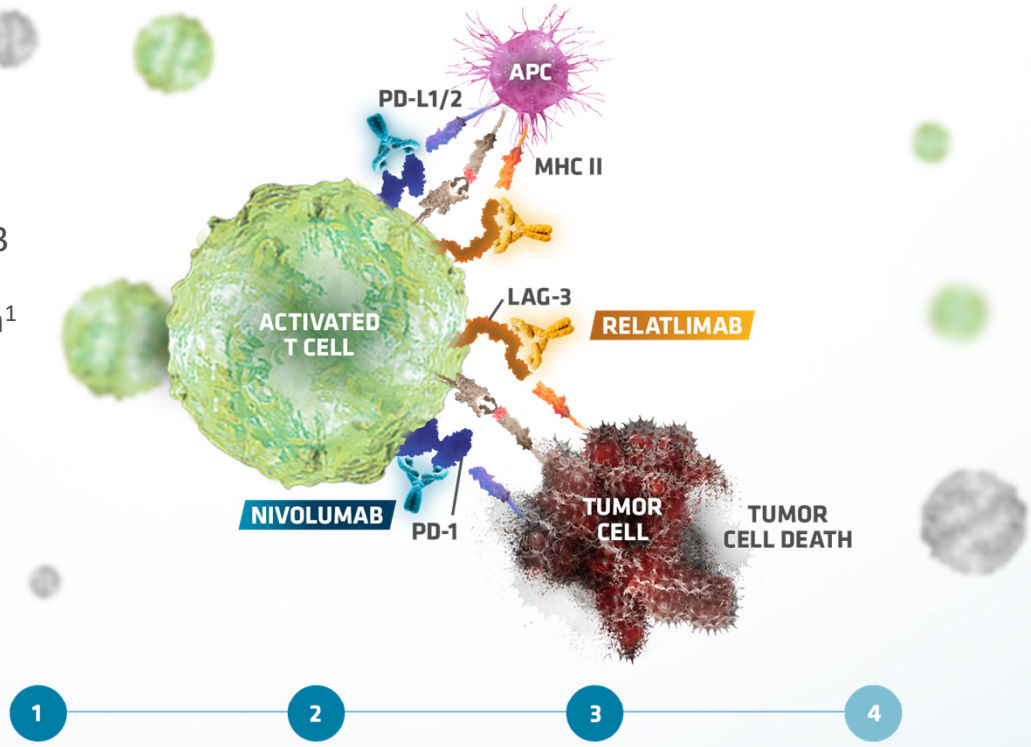


Targeting of normal cells can occur.
The illustrated mechanism of action may vary for each patient and may not directly correlate with clinical significance
APC, antigen-presenting cell; **LAG-3,** lymphocyte-activation gene 3; **MHC II,** major histocompatibility complex II; **PD-1,** programmed death receptor-1; **PD-L1,** programmed death ligand 1; **PD-L2,** programmed death ligand 2

1. SmPC Opdualag®. 2. Long L, Zhang X, Chen F, et al. The promising immune checkpoint LAG-3: from tumor microenvironment to cancer immunotherapy. *Genes Cancer*. 2018;9(5-6):176-189. 3. Hodi FS, Tawbi HA, Lipson EJ, et al. Relatlimab (RELA) + nivolumab (NIVO) versus NIVO in previously untreated metastatic or unresectable melanoma: additional efficacy in RELATIVITY-047. Oral presentation at ESMO 2021. Abstract 10360

OPDUALAG® SYNERGISTICALLY ACTS ON LAG-3 AND PD-1 TO INCREASE T-CELL ACTIVITY AND COUNTER T-CELL EXHAUSTION[1,2,3]

- LAG-3 and PD-1 are two distinct immune checkpoints[1,3]
- Relatlimab binds to the LAG-3 receptor and blocks its interaction with the ligands, including MHC II, reducing LAG-3 pathway-mediated inhibition of the immune response, thereby promoting T-cell proliferation and cytokine secretion[1]
- Nivolumab binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, thereby relieving T-cell exhaustion and improving cytokine production[1]
- The combination of nivolumab- and relatlimab-mediated inhibition increases T-cell activity compared to the activity of either antibody alone[1]



Targeting of normal cells can occur.
The illustrated mechanism of action may vary for each patient and may not directly correlate with clinical significance
APC, antigen-presenting cell; **LAG-3,** lymphocyte-activation gene 3; **MHC II,** major histocompatibility complex II; **PD-1,** programmed death receptor-1; **PD-L1,** programmed death ligand 1; **PD-L2,** programmed death ligand 2

1. SmPC Opdualag. 2. Long L, Zhang X, Chen F, et al. The promising immune checkpoint LAG-3: from tumor microenvironment to cancer immunotherapy. *Genes Cancer*. 2018;9(5-6):176-189. 3. Tawbi HA, Schadendorf D, Lipson EJ, et al. Relatlimab and nivolumab versus nivolumab in untreated advanced melanoma. *N Engl J Med*. 2022;386(1):24-34