Pomalyst® (pomalidomide), Revlimid® (lenalidomide), Thalomid® (thalidomide) – New warning

- On November 29, 2017, the FDA approved an update to the *Warnings and Precautions* section of the Pomalyst (pomalidomide), Revlimid (lenalidomide), and Thalomid (thalidomide) drug labels regarding increased mortality in patients with multiple myeloma (MM) when Keytruda® (pembrolizumab) is added to a thalidomide analogue and dexamethasone.
    - Pomalyst is indicated for use in MM.
    - Revlimid is indicated for use in MM, myelodysplastic syndromes, and mantle cell lymphoma.
    - Thalomid is indicated for use in MM and erythema nodosum leprosum.
    - Refer to the drug labels for more indication information.
- In two randomized clinical trials in patients with MM, the addition of Keytruda to a thalidomide analogue plus dexamethasone, a use for which no programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PDL1) blocking antibody is indicated, resulted in increased mortality.
- In Study KN183 (NCT02576977), patients with relapsed or refractory MM were randomized to receive Pomalyst and dexamethasone with (n = 125) or without (n = 124) Keytruda. The hazard ratio for overall survival (OS) was 1.61 (95% CI: 0.91, 2.85), increasing the relative risk of death by more than 50% in the experimental arm containing Keytruda.
    - Causes of death in the experimental arm, excluding disease progression, included: myocarditis, Stevens-Johnson syndrome, myocardial infarction, pericardial hemorrhage, cardiac failure, respiratory tract infection, neutropenic sepsis, sepsis, multiple organ dysfunction, and respiratory failure.
- In Study KN185 (NCT02579863), patients with newly diagnosed MM were randomized to receive Revlimid and dexamethasone with (n = 151) or without (n = 150) Keytruda. The hazard ratio for OS was 2.06 (95% CI: 0.93, 4.55), increasing the relative risk of death by more than 100% in the experimental arm containing Keytruda.
    - Causes of death in the experimental arm, excluding disease progression, included: intestinal ischemia, cardio-respiratory arrest, suicide, pulmonary embolism, cardiac arrest, pneumonia, sudden death, myocarditis, large intestine perforation, and cardiac failure.
- Treatment of patients with MM with a PD-1 or PDL1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.
- A similar update was recently made to the *Warnings and Precautions* section of the Keytruda drug label.
- Pomalyst, Revlimid, and Thalomid carry a boxed warning regarding embryo-fetal toxicity and venous thromboembolism.

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- The boxed warning for Pomalyst also includes arterial thromboembolism.
- The boxed warning for Revlimid also includes hematologic toxicity and arterial thromboembolism.

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