

# Utomilumab

Utomilumab is the non-proprietary name for PF-05082566, an investigational immunotherapy and fully human IgG2 monoclonal antibody (mAb).

## MECHANISM OF ACTION

The 4-1BB (CD-137) protein receptor is found on certain T cells (primarily on CD8+, but also on CD4+ memory T cells) and natural killer (NK) cells.<sup>1,2</sup> Based on preclinical data, when utomilumab (PF-05082566) binds to 4-1BB, it has been observed to stimulate and increase the number of immune cells.<sup>1</sup> The hypothesis is that this may help augment enhanced anti-tumor immune function.<sup>1</sup>



## THE POTENTIAL OF COMBINATION APPROACH

Preclinical studies suggest that combining utomilumab (PF-05082566) with a checkpoint inhibitor, such as anti-PD-1/anti-PD-L1, or other immunotherapies may amplify the immune response.<sup>4-6</sup> Further understanding the biology of how the immune system attacks tumors and ways by which tumors evade the immune system may lead to new investigational approaches.

## CLINICAL STUDIES

Pfizer is exploring the potential of utomilumab (PF-05082566) in a clinical development program to determine:

- Maximum tolerated dose
- Anti-tumor activity and safety profile
- Therapeutic potential as a single agent and in combination with other therapies

The safety and efficacy of the agent(s) under investigation have not been established. There is no guarantee that the agent(s) will receive regulatory approval and become commercially available for use(s) being investigated. All information is current as of June 2017.

## EARLY-STAGE STUDIES

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- In preclinical models, utomilumab (PF-05082566) has shown anti-tumor activity by enhancing T cell-mediated immune responses.<sup>1-3</sup>
- Data from a Phase 1 study that evaluated utomilumab (PF-05082566) in combination with rituximab in patients with relapsed or refractory CD20-positive non-Hodgkin's lymphoma (NHL) showed that utomilumab (PF-05082566) had anti-tumor activity (NCT01307267).<sup>4</sup>
  - No dose-limiting toxicities were observed, and no patients discontinued treatment due to treatment-related adverse events.
  - These results characterize the potential activity for this investigational immunotherapy when used in combination with a drug such as rituximab, which has a different MOA.
- Safety data from a Phase 1b trial of utomilumab (PF-05082566) in combination with pembrolizumab, a PD-1 inhibitor, in patients with advanced solid tumors showed that advanced solid tumors characterized an acceptable safety profile and an early indication of potential anti-tumor activity across solid tumors.<sup>5</sup>
  - Treatment-emergent adverse events did not appear to increase with higher doses of utomilumab, and no dose-limiting toxicity was reported.
  - These results warrant further investigation to confirm whether combining utomilumab with a checkpoint inhibitor may amplify anti-tumor responses.

## ONGOING STUDIES

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Pfizer is investigating utomilumab (PF-05082566) in both hematologic cancers and solid tumors in several ongoing trials as both a single agent and in combination with other anti-cancer therapies, including immunotherapies.

- A Phase 1 study as a single agent in patients with solid tumors or B-cell lymphomas, and in combination with rituximab in patients with CD20-positive non-Hodgkin's lymphoma (NHL) (NCT01307267).<sup>6</sup>
- A Phase 1b/2 study in collaboration with EMD Serono evaluating combination regimens with various agents in relapsed and refractory diffuse large B-cell lymphoma (DLBCL) (NCT02951156).<sup>7</sup>
- A Phase 1b/2 study in combination with avelumab in patients with locally advanced or metastatic solid tumors, including a triplet combination with avelumab and PF-04518600, an OX40 agonist (NCT02554812).
- A Phase 1 combination study with PF-04518600 (OX40 agonist) in patients with select advanced or metastatic cancer (NCT02315066).<sup>10</sup>

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