Sonrotoclax (BGB-11417)

Disclaimer: This asset is intended for media professionals only.
Sonrotoclax is an investigational drug for which safety and efficacy have not been established.

WHAT IS SONROTOCLAX?

Sonrotoclax is an **investigational small molecule B-cell lymphoma 2 (BCL2) inhibitor** with a differentiated profile.

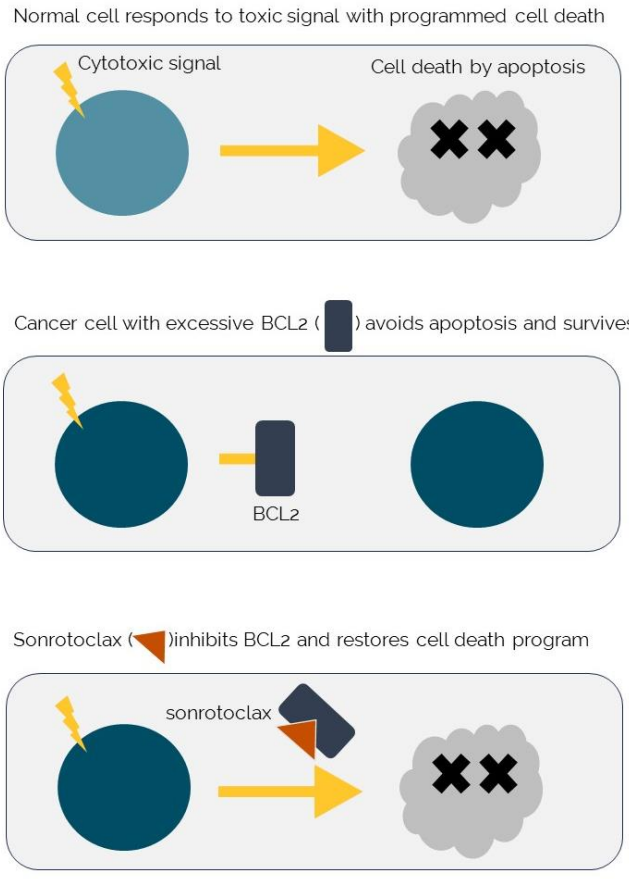
BCL2 is a member of a family of proteins that **regulate a cellular death program called apoptosis**. Certain family members activate the cell death program, while **BCL2 opposes the initiation of apoptosis and promotes cellular survival.**

Many cancer cells make abnormally high amounts of BCL2, which effectively overrides the natural apoptosis protocol, **allowing the cancer cells to survive** despite signals such as DNA damage that would otherwise trigger cancer cell destruction.

HOW SONROTOCLAX WORKS

Sonrotoclax is designed to **bind BCL2 and prevent it from blocking the apoptosis signals**. Therefore, when sonrotoclax is present, the BCL2 blockade is removed, and **the cellular self-destruction protocol proceeds to destroy cancer cells**.

Many cancer drugs act by triggering apoptosis, so blocking BCL2 with an inhibitor like sonrotoclax has the **potential to work in concert with those cancer drugs to make them more effective.**



DIFFERENTIATION: BEST-IN-CLASS POTENTIAL

The first-generation BCL2 inhibitor was approved for the treatment of patients with certain types of leukemia, but its use can be limited due to drug-related toxicities, burdensome monitoring, and resistance mutations.[1,2,3]

Sonrotoclax was designed to improve upon the first-generation BCL2 inhibitor in several ways. *In preclinical studies*:[4]

Sonrotoclax is more potent, meaning less of the drug is needed to achieve the same level of inhibition of BCL2, which may contribute to efficacy and tolerability.	**Sonrotoclax is more selective, meaning it shows a higher degree of preference for BCL2 versus other family members, making it less likely to bind to the wrong target, which may lead to a favorable safety and side effect profile.**	**Sonrotoclax has a shorter half-life, meaning it does not last as long in the body, potentially reducing or avoiding toxic drug accumulation, which may allow improved dosing protocols.**	**Sonrotoclax inhibits both unaltered BCL2 as well as a commonly mutated version of BCL2 that is resistant to inhibition by the first-generation BCL2 inhibitor.**

Disclaimer: The clinical significance of data based on non-clinical studies has not been established.

DEVELOPMENT HIGHLIGHTS

Sonrotoclax is currently in clinical development in various hematologic cancers, both in combinations with other oncology medicines and on its own as a monotherapy.

Sonrotoclax is being evaluated as part of the global Phase 3 CELESTIAL-TNCLL study (NCT06073821) – the **only fixed-duration trial combining a BCL2 inhibitor (sonrotoclax) and BTK inhibitor (zanubrutinib) designed to show superiority against a contemporary and clinically relevant comparator** (venetoclax plus obinutuzumab).

[1] Montero J, Letai A. Cell Death Differ. 2018;25:56–64
[2] Opat et al. EHA Presentation. 2022. Abstract number: P687
[3] Tausch, Eugen et al. "Venetoclax resistance and acquired BCL2 mutations in chronic lymphocytic leukemia." Haematologica vol. 104,9 (2019): e434-e437.
[4] Hu N et al. Cancer Res. 2020;80(16 Suppl):Abstract 3077, AACR 2020