

Apellis fails to complement severe Covid-19



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Hitting complement activation looks to follow inhibition of [Jak](#) and [GM-CSF](#) in being crossed off the list of mechanistic approaches to treat severe Covid-19. Yesterday Apellis said it was canning its complement C3 inhibitor APL-9 in severe Covid-19 after a phase I/II study found no meaningful reduction in mortality. This came on the heels of similar failures from Alexion's anti-C5 MAb Ultomiris and Inflarx's C5a-targeting IFX-1. Complement forms part of the innate immune response to viruses and triggers inflammation, so the idea was that inhibiting it could reduce cytokine activation and prevent lung damage, along the lines that have seen anti-IL-6 antibodies tested in Covid-19. This was backed by mouse studies showing that activation of complement C3 exacerbated disease in Sars, and as early as February 2020 Alexion was proposing to use Soliris to manage severe pneumonia associated with Covid-19. Given the successes of antibodies, not to mention vaccine roll-outs, the failure of the complement mechanism probably matters little at this stage, but it does leave up in the air the fate of ongoing complement inhibitor trials being run by UCB, Innate Pharma and Pharming.

Selected complement inhibitors against Covid-19

Project	Mechanism	Company	Status
Soliris	Anti-complement factor C5 MAb	Alexion	Available under expanded access programme
IFX-1	Anti-complement factor C5a MAb	Inflarx	Failed clinical trial in Dec 2020
Ultomiris	Anti-complement factor C5 MAb	Alexion	Failed clinical trial in Jan 2021
APL-9	Complement factor C3 inhibitor	Apellis	Failed clinical trial in Mar 2021
Zilucoplan	Complement factor C5 inhibitor	UCB	Ph2 trial ended Dec 2020; results imminent
Avdoralimab	Anti-complement factor C5a MAb	Novo Nordisk/Innate Pharma	Ph2 trial ends Mar 2021
Ruconest	C1 esterase inhibitor	Pharming	Ph2 trial ends Aug 2021
AMY-101	Complement factor C3 inhibitor	Amyndas	Ph2 trial not yet recruiting
Coversin	Complement factor C5a & C5b-9 inhibitor	Akari	Trial cleared in Oct 2020, but not yet begun

Source: [clinicaltrials.gov](#) & company statements.

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