Optimizing Novel Therapeutics Targeting Cytomegalovirus Entry To Effectively Inhibit Virus Proliferation

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Cytomegalovirus (CMV) is a betaherpesvirus that is typically latent in a human host, but presents dangerously in immunocompromised patient populations. CMV primary infection or reactivation from latency can cause birth defects, vision loss, and nervous system problems. Current successful CMV treatments include the drug ganciclovir and antibody CMV hyperimmune globulin, which target the late-stage of virus replication, but are associated with toxicity and severe inflammation, as high doses are necessary according to current literature.Thus, CMV continues to be a major medical need for safe and effective therapeutics to prevent and treat CMV diseases. A promising novel approach is to develop diverse therapeutics to the early phase of virus entry. Previous studies have identified a monoclonal antibody directed to a CMV envelope protein and a chemical molecule that blocks CMV infection. I evaluated the ability of the novel human monoclonal antibody 1C10 and chemical inhibitor N-arylpyrimidineamine (MBX-4992) to limit virus proliferation by blocking entry level infection. These assays will define treatment conditions, therapeutic durability, and determine an effective dosage of 1C10 and MBX. I found that the lowest dose of each therapeutic was effective at inhibiting CMV proliferation and preventing spread as effectively as current treatment options, using up to 96% less therapeutic over a short-term treatment period. These results support the model that blocking virus entry has a dramatic impact on CMV spread. My findings highlight biologics 1C10 and MBX-4992 as suitable alternatives to FDA-approved ganciclovir and CMV hyperimmune globulin to treat diverse immunocompromised patient populations with novel specificity, aiming to reduce additional morbidity.

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