An imbalance between production and clearance of the amyloid-β peptide (Aβ) is a key momentum of the complex pathological cascade of Alzheimer’s disease (AD). It is caused by overproduction of Aβ or, more frequently, by impaired clearance from brain. Clearance can be reduced by increased aggregation, defective degradation, disturbed balance of transport across the blood-brain barrier, or inefficient peripheral removal of the peptide. In recent years these mechanisms have become targets of pharmacological interventions. Although several compounds have been discarded on the grounds of limited clinical efficacy, all major clearance-related approaches still hold promise. Some drug candidates have advanced to Phase III trials including anti-Aβ antibodies, metal complexing agents, ginseng extracts, and intravenous immunoglobulins. Data are currently not available from these studies that might allow an evaluation of efficacy and safety. Phase II trials on active and passive immunization have demonstrated a striking discrepancy between significant neurobiological effects regarding the removal of Aβ deposits and minor clinical outcomes. This does not preclude the possibility that clearance-related strategies have the potential of saving neurons and synapses via reducing the levels of soluble and particularly toxic Aβ species in brain. It may take longer than projected in ongoing trials for such neurobiological effects to translate into measurable changes of clinical progression.