A Comparison of Cancer Immunotherapy Approaches

BiTEs/TriTEs
T and NK cell engagers

CAR-T Therapy
Engineered T cells

ADCs
Antibody-Drug Conjugates

Checkpoint Inhibitors
Immune restoration

Core Mechanism	Bispecific/trispecific Ab bridges T (CD3) or NK cell to tumor antigen	Patient/donor T cells engineered to express chimeric antigen receptor targeting TAA	Antibody delivers cytotoxic payload directly to antigen-positive tumor cells	Blocks inhibitory receptor-ligand interactions (PD-1/PD-L1) to restore endogenous T cell activity
Effector Cell Source	Patient's own circulating T/NK cells (redirected in situ)	Ex vivo engineered autologous or allogeneic T cells	None — direct cytotoxic/chemical killing	Patient's own pre-existing tumor-reactive T cells
Target Recognition	Antigen-dependent, MHC-independent	Antigen-dependent, MHC-independent	Surface antigen-dependent	TCR-dependent (requires neoantigen/MHC presentation)
Manufacturing	Off-the-shelf, standard biologic production	Patient-specific (or allogeneic), complex cell manufacturing, weeks-long turnaround	Off-the-shelf, standard biologic-chemical conjugation	Off-the-shelf, standard biologic production
Dosing	Continuous infusion or repeated dosing (SC options emerging)	Single infusion (living drug, self-amplifying)	Repeated IV dosing on a cycle	Repeated IV/SC dosing on a cycle
Onset of Action	Rapid	Rapid to delayed (expansion phase needed)	Moderate (dependent on payload release/PK)	Delayed (immune priming required)
Key Toxicities	Cytokine release syndrome (CRS), neurotoxicity (ICANS)	CRS, ICANS (often more severe/prolonged)	Payload-related (myelosuppression, ocular, neuropathy)	Immune-related adverse events (colitis, pneumonitis, endocrinopathies)
Antigen Escape Risk	Moderate–high (single/dual antigen dependent)	High (well-documented antigen loss relapse)	Moderate (target downregulation)	Low direct risk (not antigen-restricted)
Tumor Microenvironment Dependence	Low–moderate	Moderate–high (trafficking/persistence issues in solid tumors)	Low (payload acts locally once internalized)	High (requires TME with active/reactivatable T cells)
Solid Tumor Efficacy (current)	Emerging (DLL3, HER2, MUC16 programs)	Limited (trafficking, exhaustion, TME hostility)	Established (HER2, TROP2, Nectin-4 targets)	Established across many indications
Hematologic Malignancy Efficacy	Strong, multiple approvals (CD19, BCMA, CD20, GPRC5D)	Strong, multiple approvals (CD19, BCMA)	Established (CD30, CD22, CD79b targets)	Limited (lower mutational burden/antigenicity)
Persistence/Durability	Requires ongoing dosing; no cellular memory	Potential for durable remission via T cell persistence/memory	Requires ongoing dosing; no memory	Can generate durable, memory-driven responses
Combinability	With checkpoint or costimulatory arms (trispecific)	With checkpoint inhibitors post-infusion	With checkpoint inhibitors, other ADCs	With chemo, ADCs, engagers, CTLA-4/LAG-3 blockade
Representative Examples	Blinatumomab, teclistamab, glofitamab, tarlatamab	Tisagenlecleucel, axicabtagene ciloleucel, ciltacabtagene autoleucel	Trastuzumab deruxtecan, brentuximab vedotin, sacituzumab govitecan	Pembrolizumab, nivolumab, ipilimumab, atezolizumab

In brief: BiTEs/TriTEs and CAR-T both redirect T/NK cells but differ in manufacturing complexity and durability; ADCs deliver cytotoxic payloads without relying on immune effector engagement; checkpoint inhibitors amplify pre-existing anti-tumor immunity rather than redirecting new killing activity. Increasingly, these modalities are used in combination rather than isolation.

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