Table 1 Preclinical studies using OV-loaded human MSCs for cancer treatment

MSCs source	Oncolytic Virus	Transgene/modification	Model	Cell line	Route	Outcomes	Reference
BM-MSCs	MYXV (vMyx-IL15Ra-tdTr)	IL-15	Lung melanoma/C57BL/6 mice	B16-F10	iv x2	Correct viral infection and progeny production Strong anti-tumor effect Production of pro-inflammatory cytokines and tumor infiltration of effector T cells	Jazowiecka-Rakus et al. (2020)
BM-MSCs	Ad (oAd/RLX-PCDP)	relaxin/polimer PCDP	Pancreatic xenograft/nude mice	AsPC-1	iv x3	Correct viral infection and progeny production Higher antitumor effect than naked OAd	Na et al. (2019)
BM-MSCs	Ad (oAd-WNTi)	Wnt-inhibiting decoy receptor (WNTi)	Orthotopic hepatocellular carcinoma/nude mice	Hep3B	iv x2	Correct viral infection and progeny production Higher antitumor effect than naked OAd MSCs improve OAdv pharmacokinetics and tumor delivery MSCs prevent hepatic damage	Yoon et al. (2019)
						MOI used to infect MSCs has a critical impact in the therapy outcome The most OAdv-MSCs used, the higher antitumor effect	Mahasa et al. (2020)
MenSCs	Ad (CRAd5/F11)	Type 11 adenovirus fiber	Colorectal cancer xenograft/nude mice	SW620	iv x2	Correct viral infection and progeny production Viral tumor delivery	Guo et al. (2019)
MenSCs	Ad (ICOVIR15)	Modified E1a promoter, delta-24, RGD	Lung adenocarcinoma xenograft/nude mice	A549	ip single	Correct viral infection and progeny production Tumor homing	Moreno et al. (2017)
MenSCs	Ad (ICOVIR15)	Modified E1a promoter, delta-24, RGD	Lung adenocarcinoma and epidermoid carcinoma xenograft/NSG mice	A549/A431	ip single	MSCs shift towards a pro-inflammatory phenotype after OAdv infection OAdv-MSCs activate allogeneic T-cells and NK-cells Benefits of using allogeneic MSCs in the presence of human immune system	Moreno et al. (2019)
MenSCs	Ad (ICOVIR15-cBiTE)	Modified E1a promoter, delta-24, RGD, EGFR-targeting bispecific T-cell engager (cBiTE)	Lung adenocarcinoma xenograft/NSG mice	A549	ip single	OAdv tumor delivery Higher antitumor effect than naked OAd Tumor T-cell recruitment through cBiTE production	Barlabé et al. (2020)
MSCs	HSV	-	Melanoma brain metastasi/SCID mice	MeWo/M12	ica single	Correct viral infection and progeny production Brain tumor metastasis homing Antitumor efficacy	Du et al. (2017)
HU-MSCs	Ad (AdAFPp-E1A-122)	alpha-fetoprotein promoter, microRNA-122	Orthotopic hepatocellular carcinoma/nude mice	HepG2	iv x2	Correct viral infection and progeny production Tumor homing MSCs prevent hepatic damage Antitumor efficacy	Yuan et al. (2016)
HU-MSCs	Ad (Ad-hTERTp-IL24)	deltaE1A, hTERT promoter, IL-24	Hepatocellular carcinoma xenograft/nude mice	HepG2	iv single	Tumor migration Tumor growth inhibition	Li et al. (2016)
BM-MSCs	Ad (Ad5/3-TRAIL)	delta-24, E3-deletion, 5/3 chimeric fiber, TRAIL,	xenograft/chick embryos	MIA-PaCa2	intramembrane	Tumor-specific migration Tumor volume reduction	Kaczorowski et al. (2016)
FM-MSCs	HSV (R-LM249)	single-chain antibody to HER-2	Lung and brain metastases, nude/NSG mice	SK-OV-3, MDA-MB-453	iv single	Correct viral infection and progeny production Anti-tumor activity against lung and brain metastasis	Leoni et al. (2015)
BM-MSCs	Ad (ICOVIR15-Ad.iC9)	Modified E1a promoter, delta-24, RGD iCaspase-9	Lung cancer xenograft/SCID-beige mice	A549	iv single	Correct viral infection and progeny production Viral tumor delivery Enhanced tumor control and mice survival	Hoyos et al. (2015)
BM-MSCs	MV	-	lymphoblastic leukemia/SCID mice	Nalm-6	iv single	Correct viral infection and progeny production Tumor target in the present of anti-MV humoral immunity Enhanced therapeutic efficacy in the presence of anti-MV antibodies	Castleton et al. (2014)
BM-MSCs	MV	-	Orthotopic hepatocellular carcinoma/SCID mice	Patient derived HCC	iv single	Correct viral infection and progeny production Tumor target in the present of anti-MV humoral immunity Enhanced therapeutic efficacy in the presence of anti-MV antibodies	Ong et al (2013)
BM-MSCs	Ad (CRAd-EGFP)	E1B-55KD deletion	Colon cancer xenograft/nude mice	HT29	ip single	Hypoxic culture increases MSCs tumor migration via CXCR4 and CX3CR1 Hypoxic MSCs support CRAd replication MSCs protect CRAd from anti-adenovirus NAbs	Huang et al (2013)
BM-MSCs	Ad (delta-24-RGD)	delta-24, RGD	Glioma stem cells xenograft	Glioma stem cells (GSC)	ica/ia single	TGF-β mediates homing of MSCs to glioma Survival enhanced	Shinojima et al. (2013)
ASCs	MV	-	Ovarian tumor xenograft/nude mice	SK-OV-3	ip single	MV infected MSCs increase survival in the presence of anti-MV immunity	Mader et al. (2009, 2013)
BM-MSCs	Ad (Ad-hOC-E1)	bidirectional human osteocalcin promoter driving E1A and E1B genes	Orthotopoic renal cell carcinoma/nude mice	RCC	ip single	PDGF-AA identified as responsible for MSCs tumor recruitment	Hsiao et al. (2012)
BM-MSCs	Ad (Ad5/3-kBF512HRE-E1Awt)	secreted protein acidic and rich cystein (SPARC) promoter, hipoxia inducible factor (HIF) and NF-kB responsive motives	Melanoma xenograft/nude mice	A375N	ro single	A specific MSCs subpopulation described with enhanced tumor migration capacity (α 2,3 and 5-integrins overexpressed) Inhibitory effect on tumor growth	Bolontrade et al. (2012)
ASCs	MYXV (vMyxgfp)	green fluorescent protein	Orthotopic brain tumor/nude mice	U87	ic single	Correct viral infection and progeny production Tumor tropism Enhanced therapeutic efficacy	Josiah et al. (2010)
BM-MSCs	Ad (delta-24-RGD)	delta-24, RGD	Intracranial glioma xenograft/nude mice	U87, U251-V121	ica single	Correct viral infection and progeny production Viral tumor delivery Tumor growth inhibition and improved survival	Yong et al. (2009)
BM-MSCs	Ad (Ad5.pK7-delta24)	seven polylysines at the COOH terminus, delta-24	Orthotopic lung and breast tumor/nude mice	LNM35, M4A4-LM3	iv single	Viral tumor delivery Tumor growth inhibition and improved survival	Hakkarainen et al. (2007)
hMSCs	Ad (Ad5/3.CXCR4)	CXCR4 promoter driving E1A, chimeric fiber 5/3	Lung metastases, SCID mice	MDA-MB-231	iv single	Tumor-specific migration Tumor growth reduction and improved mice survival	Stoff-Khalili et al. (2007)

BM-MSCs: bone marrow-MSCs; MenSCs: menstrual blood-derived MSCs; HU-MSCs: umbilical cord-derived MSCs; FM-MSCs: fetal membrane MSCs; ASCs: adipose-derived MSCs
MYXV: myxoma virus; Ad: adenovirus; OAd: oncolytic adenovirus; HSV: herpes simplex virus; MV: measles virus
iv: intravenous; ip: intraperitoneal; ica: intracarotid; ia:intra-arterial; ro: retro-orbital; ic: intracraneal
EGFR: epidermal growth factor receptor; NSG: NOD scid gamma; SCID: severe combined immunodeficient; HCC: hepatocellular carcinoma; NAbs: neutralizing antibodies; PDGF-AA: platelet derived growth factor AA