

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	Jazowiecka-Rakus et al. (2020)
BM-MSCs	Ad (oAd/RLX-PCDP)	relaxin/polymer PCDP	Pancreatic xenograft/nude mice	AsPC-1	iv x3	Production of pro-inflammatory cytokines and tumor infiltration of effector T cells Correct viral infection and progeny production	Na et al. (2019)
BM-MSCs	Ad (oAd-WNT1)	Wnt-inhibiting decoy receptor (WNT1)	Orthotopic hepatocellular carcinoma/nude mice	Hep3B	iv x2	Higher antitumor effect than naked OAd Correct viral infection and progeny production	Yoon et al. (2019)
MenSCs	Ad (CRAAd5/F11)	Type 11 adenovirus fiber	Colorectal cancer xenograft/nude mice	SW620	iv x2	MSCs improve OAdv pharmacokinetics and tumor delivery MSCs prevent hepatic damage	Mahasa et al. (2020)
MenSCs	Ad (ICOVIR15)	Modified E1a promoter, delta-24, RGD	Lung adenocarcinoma xenograft/nude mice	A549	ip single	MOI used to infect MSCs has a critical impact in the therapy outcome The most OAdv-MSCs used, the higher antitumor effect	Guo et al. (2019)
MenSCs	Ad (ICOVIR15)	Modified E1a promoter, delta-24, RGD	Lung adenocarcinoma and epidermoid carcinoma xenograft/NSG mice	A549/A431	ip single	Correct viral infection and progeny production Viral tumor delivery	Moreno et al. (2017)
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	Tumor homing MSCs shift towards a pro-inflammatory phenotype after OAdv infection	Moreno et al. (2019)
MSCs	HSV	-	Melanoma brain metastasi/SCID mice	MeWo/M12	ica single	OAdv-MSCs activate allogeneic T-cells and NK-cells Benefits of using allogeneic MSCs in the presence of human immune system OAdv tumor delivery	Barlabé et al. (2020)
HU-MSCs	Ad (AdAFPp-E1A-122)	alpha-fetoprotein promoter, microRNA-122	Orthotopic hepatocellular carcinoma/nude mice	HepG2	iv x2	Higher antitumor effect than naked OAd Tumor T-cell recruitment through cBITE production	Du et al. (2017)
HU-MSCs	Ad (Ad-hTERTp-IL24)	deltaE1A, hTERT promoter, IL-24	Hepatocellular carcinoma xenograft/nude mice	HepG2	iv single	Correct viral infection and progeny production Brain tumor metastasis homing Antitumor efficacy	Yuan 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 homing MSCs prevent hepatic damage Antitumor efficacy	Li 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	Tumor migration Tumor growth inhibition	Kaczorowski et al. (2016)
BM-MSCs	Ad (ICOVIR15-Ad.iC9)	Modified E1a promoter, delta-24, RGD iCaspase-9	Lung cancer xenograft/SCID-beige mice	A549	iv single	Tumor-specific migration Tumor volume reduction	Leoni et al. (2015)
BM-MSCs	MV	-	lymphoblastic leukemia/SCID mice	Nalm-6	iv single	Correct viral infection and progeny production Anti-tumor activity against lung and brain metastasis	Hoyos et al. (2015)
BM-MSCs	MV	-	Orthotopic hepatocellular carcinoma/SCID mice	Patient derived HCC	iv single	Enhanced tumor control and mice survival Correct viral infection and progeny production	Castleton et al. (2014)
BM-MSCs	Ad (CRAAd-EGFP)	E1B-55KD deletion	Colon cancer xenograft/nude mice	HT29	ip single	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 (delta-24-RGD)	delta-24, RGD	Glioma stem cells xenograft	Glioma stem cells (GSC)	ica/ia 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	Huang et al. (2013)
ASCs	MV	-	Ovarian tumor xenograft/nude mice	SK-OV-3	ip single	Hypoxic culture increases MSCs tumor migration via CXCR4 and CX3CR1 Hypoxic MSCs support CRAd replication MSCs protect CRAd from anti-adenovirus NAb	Shinojima et al. (2013)
BM-MSCs	Ad (Ad-hOC-E1)	bidirectional human osteocalcin promoter driving E1A and E1B genes	Orthotopic renal cell carcinoma/nude mice	RCC	ip single	TGF-β mediates homing of MSCs to glioma Survival enhanced	Mader et al. (2009, 2013)
BM-MSCs	Ad (Ad5/3-kBF512HRE-E1Awt)	secreted protein acidic and rich cystein (SPARC) promoter, hypoxia inducible factor (HIF) and NF-κB responsive motives	Melanoma xenograft/nude mice	A375N	ro single	MV infected MSCs increase survival in the presence of anti-MV immunity	Hsiao et al. (2012)
ASCs	MYXV (vMyxgfp)	green fluorescent protein	Orthotopic brain tumor/nude mice	U87	ic 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)
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	Josiah et al. (2010)
BM-MSCs	Ad (Ad5.pK7-delta24)	seven polylysines at the COOH terminus, delta-24	Orthotopic lung and breast tumor/nude mice	LN35, M4A4-LM3	iv single	Enhanced therapeutic efficacy Correct viral infection and progeny production	Yong et al. (2009)
hMSCs	Ad (Ad5/3.CXCR4)	CXCR4 promoter driving E1A, chimeric fiber 5/3	Lung metastases, SCID mice	MDA-MB-231	iv single	Viral tumor delivery Tumor growth inhibition and improved survival	Hakkaraianen et al. (2007)
						Tumor growth inhibition and improved survival 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: intracardial; ia: intra-arterial; ro: retro-orbital; ic: intracranial

EGFR: epidermal growth factor receptor; NSG: NOD scid gamma; SCID: severe combined immunodeficient; HCC: hepatocellular carcinoma; NAb: neutralizing antibodies; PDGF-AA: platelet derived growth factor AA