

## Supplementary Materials: TP53 in Biology and Treatment of Osteosarcoma

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**Table S1.** List of missense mutations in the *TP53* gene founded in osteosarcoma derived patients samples. Description possess number of exon in which mutation is localize, codon number and literature reference. Abbreviation used are: Ref. for aminoacid which was changed and Alt. for altered aminoacid.

EXON	REF.	CODON	ALT.	LITERATURE
2	D	7	N	[79]
3	R	26	W	[79]
4	P	47	L / S	[80], [81]
4	P	72	R	[81]
4	Y	107	H	[81]
4	G	108	S	[81]
5	S	127	P	[82]
5	C	135	Y / F / R / W	[79], [83]
5	V	147	D	[79]
5	P	151	A	[81]
5	V	157	F	[83]
5	A	159	N	[84]
5	Y	163	C	[79]
5	V	172	N	[80]
5	V	173	M / G / L	[82,85], [79]
5	R	175	H	[79-81,85-87]
5	H	179	Q / Y	[88], [89]
5	R	181	P	[80]
5	S	185	N	[81]
6	H	193	Q / Y	[86,90], [83]
6	V	197	G	[80]
6	Y	205	C	[80,88,91]
6	S	215	I	[79]

6	Y	220	C	[80,83,85]
6	E	224	D	[85,89]
7	N	235	S	[81]
7	Y	236	C	[83]
7	M	237	I	[79,80,91]
7	C	238	F / G / Y	[79,92], [80]
7	S	241	Y	[86]
7	C	242	Y / R	[80-82], [81]
7	G	244	V	[86]
7	G	245	S / D	[80], [89]
7	M	246	T	[81]
7	R	248	Q / W / G	[80-83,88,89,91], [79,80,89], [83]
7	R	249	T	[82]
7	P	250	I / L / F	[80], [86,90], [87]
7	I	255	T / F	[92], [79]
7	T	256	S / P	[80,91], [82,83]
7	L	257	R	[83]
7	D	259	V	[86]
8	R	267	W	[82]
8	N	268	S	[87]
8	V	272	M	[85]
8	R	273	H / L / C	[80-82,85-90], [79,92], [85]
8	C	275	Y	[79,82,92]
8	A	276	P / G	[89], [79]
8	C	277	F	[82]
8	P	278	A	[81]
8	R	280	H	[80]
8	D	281	E / N / H / V	[79,83,90,92], [80,86,90], [80,85,86,90], [82,83]

8	R	282	Q / W	[89], [81,83]
8	E	285	K	[80,88]
8	E	286	K	[81]
8	R	290	C	[82]
8	E	298	K	[81]
10	R	337	H / C / L	[82,88], [79,80,83], [82]

**Table S2.** Overview of clinical trials retrieved from ClinicalTrials.gov and EU Clinical Trials Register. The search was performed with keywords: p53, gene therapy. Trials with status “withdrawn” were excluded. Databases accessed on 10/22/2020.

Trial No.	Condition/group of patients	Administered agent	Phase	Start (year)	Status	Enrollment	Locations
NCT02561546	Diabetes concurrent with Hepatocellular carcinoma (HCC).	p53 gene therapy, Trans-catheter embolization (TAE)	2	2015	Unknown	40	China, Liaoning first affiliated hospital in Dalian University Dalian, Liaoning, China
NCT02509169	Advanced Hepatocellular Carcinoma (HCC)	TAE plus P53 gene therapy	2	2014	Unknown	60	China, Liaoning first affiliated hospital in Dalian University Dalian, Liaoning, China
NCT01574729	Non-small Cell Lung Cancer	Surgery combined with rAd-p53 gene therapy	2	2012	Unknown	120	Institute of Surgery Research, Daping Hospital, Third Military Medical University Chongqing, Chongqing, China
NCT02435186	Ovarian Epithelial Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer	p53 gene, Cisplatin, Paclitaxel	2	2015	Unknown	100	Xijing Hospital in China Medical University Shenyang Liaoning, China,
NCT00902083	Advanced Oral and Maxillofacial Malignant Tumors	-p53 gene with surgery -p53 gene with standard chemotherapy -p53 gene therapy	4	2009	Unknown	600	West China Hospital, Sichuan University Chengdu, Sichuan, China
NCT02429037	Advanced Head and Neck Cancer	- radiation and Cisplatin -rAd-p53 and radiation and Cisplatin	2	2015	Unknown	60	Jiangsu cancer hospital Nanjing, Jiangsu, China

NCT00902122	Advanced Malignant Thyroid Tumors	-rAd-p53 - rAd-p53 with surgery -rAd-p53 with radioactive iodine	4	2009	Unknown	600	West China Hospital, Sichuan University Chengdu, Sichuan, China
NCT02429726	Malignant Pleural Effusion	-rAdp53 -Cisplating - rAdp53 plus cisplatin	2	2015	Unknown	90	The First Affiliated Hospital of Xi'an Jiao Tong University Xian, Shanxi, China
NCT00064103	-Lip and Oral Cavity Cancer -Oropharyngeal Cancer Stage 0 -Lip and Oral Cavity Cancer Stage 0 -Oropharyngeal Cancer -Tongue Cancer	Ad5CMV-p53 gene	2	2003	Completed	51	M D Anderson Cancer Center Houston, Texas, United States
NCT02418988	Advanced Adult Hepatocellular Carcinoma	-TACE plus rAd-p53 artery injection - TACE	2	2014	Unknown	120	China, Shanxi Xijing Hospital of the Fourth Military Medical University Xi An, Shanxi, China

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NCT00001827	Ovarian Neoplasm	-Aldesleukin -incomplete Freund's adjuvant -p53 peptide vaccine -Sargramostim -therapeutic autologous dendritic cells Procedure: in vitro-treated peripheral blood stem cell transplantation	2	1999	Terminated	21	United States, Maryland National Institutes of Health Clinical Center, Bethesda, Maryland, United States
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NCT01191684	Recurrent Colon Cancer	modified vaccinia virus ankara vaccine expressing p53	1	2011	Completed	12	City of Hope Medical Center Duarte, California, United States
	Recurrent Gastric Cancer						
	Recurrent Pancreatic Cancer						
	Recurrent Rectal Cancer						
	Stage III Colon Cancer						
	Stage III Gastric Cancer						
	Stage III Pancreatic Cancer						
	Stage III Rectal Cancer						
	Stage IV Colon Cancer						
	Stage IV Gastric Cancer						
	Stage IV Pancreatic Cancer						
	Stage IV Rectal Cancer						
NCT00003450	Ovarian Cancer Peritoneal Cavity Cancer	Ad5CMV-p53 gene	1	1998	Completed	15-20	Simmons Cancer Center - Dallas Dallas, Texas, United States

NCT00894153	head and neck malignant tumors in advanced stage	-rAd-p53 intra-tumor injection - rAd-p53 intra-tumor injection plus chemotherapy - rAd-p53 intra-tumor injection plus radiotherapy - rAd-p53 intra-tumor injection plus surgery	4	2009	Unknown	1200	Department of oral and maxillofacial surgery, Huaxi university of medical science Chendu, Shichuan, China
NCT00004041	Brain and Central Nervous System Tumors	intratumoral stereotactic injection of adenovirus p53 (Ad-p53)	1	1999	Completed	30	UCSF Cancer Center and Cancer Research Institute San Francisco, California, United States
NCT00004038	Breast Cancer	Ad5CMV-p53 gene plus chemotherapy	1	1999	Completed	20	Fox Chase Cancer Center Philadelphia, Pennsylvania, United States
NCT00003147	Liver Cancer	Ad5CMV-p53 gene	1	1998	Terminated	30	Albert Einstein Comprehensive Cancer Center Bronx, New York, United States
NCT00410865	Mouth Cancer	INGN 201 (Ad-p53 gene)	1	2003	Terminated	4	UT MD Anderson Cancer Center Houston, Texas, United States



NCT00003167	-Recurrent Bladder Cancer: -Stage I -Stage II - Stage III - Stage IV -Transitional Cell Carcinoma of the Bladder	Ad5CMV-p53 gene	1	1998	Completed	24	M D Anderson Cancer Center Houston, Texas, United States
NCT00003649	Lung Cancer	Ad5CMV-p53 gene	1	1998	Completed	15	Veterans Affairs Medical Center - Tennessee Valley Healthcare System - Nashville Campus Nashville, Tennessee, United States Vanderbilt-Ingram Cancer Center Nashville, Tennessee, United States
NCT00003588	Ovarian Cancer	Ad5CMV-p53 gene (laparoscopic surgery)	1	1998	Completed	30	University of Texas - MD Anderson Cancer Center Houston, Texas, United States
NCT03544723	Solid Tumor Lymphoma	Ad-p53	2	2018	Recruiting	40	Robert H. Lurie Comprehensive Cancer Center   Northwestern University Chicago, Illinois, United States

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							Sidney Kimmel Cancer Center San Diego, California, United States,
							University of Colorado Cancer Center Denver, Colorado, United States
							University of Connecticut School of Medicine Farmington, Connecticut, United States
							Clinical Sciences Building Chicago, Illinois, United States
							University of Iowa Hospitals and Clinics Iowa City, Iowa, United States
NCT00003257	Head and Neck Cancer	Ad5CMV-p53 gene	2	1998	Unknown	39	University of Kansas Medical Center Kansas City, Kansas, United States
							Tulane University School of Medicine New Orleans, Louisiana, United States
							Marlene & Stewart Greenebaum Cancer Center, Uni- versity of Maryland Baltimore, Maryland, United States
							Albert Einstein Comprehensive Cancer Center Bronx, New York, United States
							Simmons Cancer Center - Dallas Dallas, Texas, United States

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NCT00017173	Head and Neck Cancer	Ad5CMV-p53 gene, cisplatin, conventional surgery, radiation therapy	2	2003	Terminated	13	Kansas Masonic Cancer Research Institute at the University of Kansas Medical Center Kansas City, Kansas, United States
							Markey Cancer Center at University of Kentucky Chandler Medical Center Lexington, Kentucky, United States
							Barbara Ann Karmanos Cancer Institute Detroit, Michigan, United States
NCT02340156	Recurrent Glioblastoma	SGT53, Temozolomide	2	2014	Terminated	1	MD Anderson Cancer Center Houston, Texas, United States
							China Medical University Hospital Taichung, Taiwan
NCT02340117	Metastatic Pancreatic Cancer	SGT-53,nab-paclitaxel, Gemcitabine	2	2015	Recruiting	28	Mary Crowley Cancer Research Center Dallas, Texas, United States
NCT00049218	Lung Cancer	Autologous dendritic cell-adenovirus p53 vaccine, Carboplatin, Etoposide	2	2003	Completed	56	H. Lee Moffitt Cancer Center and Research Institute Tampa, Florida, United States
NCT00617409	Small Cell Lung Cancer	Paclitaxel, Ad.p53-DC vaccines, All-trans Retinoic Acid (ATRA)	2	2007	Completed	69	H. Lee Moffitt Cancer Center & Research Institute Tampa, Florida, United States

NCT00004225	Lung Cancer	Ad5CMV-p53 gene plus radiation therapy	1	2000	Completed	10	Vanderbilt-Ingram Cancer Center at Vanderbilt Medical Center Nashville, Tennessee, United States
NCT00044993	Breast Cancer	-Ad5CMV-p53 gene plus docetaxel plus doxorubicin hydrochloride -conventional surgery (neoadjuvant therapy)	2	2002	Completed	60	University of Texas - MD Anderson Cancer Center Houston, Texas, United States
NCT00393029	Metastatic Cancer That Overexpresses p53 Using Lymphodepleting Conditioning Followed by Infusion of Anti-p53 T Cell Receptor (TCR)-Gene Engineered Lymphocytes	-Anti-protein 53 or tumor protein 53 (p53) T-cell receptor transduced peripheral blood lymphocytes -Aldesleukin -Filgrastim -Cyclophosphamide -fludarabine phosphate	2	2006	Completed	12	National Institutes of Health Bethesda, Maryland, United States
NCT00004080	Brain and Central Nervous System Tumors (recurrent and progressive)	-recombinant adenovirus-p53 SCH-58500 conventional surgery	1	1999	Completed	21-42	Emory University, Atlanta, United States

NCT00002960	Fallopian Tube Cancer Metastatic Cancer Ovarian Cancer Primary Peritoneal Cavity Cancer	recombinant adenovirus-p53 SCH-58500	1	1999	Completed	59	Merck Sharp & Dohme Corp., United States, Germany
NCT00041613	Carcinoma, Squamous Cell	INGN 201	3		Unknown		University of Colorado Cancer Center Aurora, Colorado, United States
NCT00041626	Carcinoma, Squamous Cell	INGN 201	3		Unknown		University of Arkansas, Little Rock, Arkansas, United States
NCT00776295	Small Cell Lung Cancer	Combined adenovirus vectored p53 transfected dendritic cell vaccine and ex vivo expanded T-lymphocytes	2	2007	Terminated	2	H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida, USA
NCT02275039	Recurrent Ovarian Epithelial Cancer Recurrent Fallopian Tube Carcinoma Recurrent Primary Peritoneal Carcinoma	-modified vaccinia virus ankara vaccine expressing p53-gemcitabine hydrochloride	1	2015	Completed	12	City of Hope Medical Center Duarte, California, United States
NCT00844506	Ovarian Cancer	P53-SLP vaccine Cyclophosphamide	2	2008	Completed	19	University Medical Centre Groningen Groningen, Netherlands

NCT03406715	Small Cell Lung Cancer Lung Cancer Relapsed Small Cell Lung Cancer	Nivolumab Ipilimumab Dendritic Cell based <b>p53</b> Vaccine	2	2018	Active, not recruiting	14	H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, United States
							Centre Léon Bérard Lyon, France
NCT04116541	Malignant Solid Tumor	HDM201 Ribociclib Cabozantinib Alectinib	2	2020	Recruiting	100	Institut Paoli Calmettes Marseille, France Centre Antoine LACASSAGNE Nice, France Institute Curie Paris, France Institute Claudius Regaud Toulouse, France
							The Angeles Clinic and Research Institute Los Angeles, California, United States MD Anderson Cancer Center Orlando Orlando, Florida, United States Emory University Atlanta, Georgia, United States, United States, Illinois
NCT01029873	Metastatic Melanoma	Cisplatin ALT-801	1 2	2010	Completed	25	Northwestern University Chicago, Illinois, United States United States, Iowa University of Iowa Hospitals and Clinics United States, Iowa Iowa City, Iowa, United States, University of Iowa Hospitals and Clinics United States, North Carolina Iowa City, Iowa, United States

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Carolinas Medical Center-Brumenthal Cancer Center  
United States, North Carolina

Carolinas Medical Center-Brumenthal Cancer Center,  
Charlotte, North Carolina, United States,

St. Luke's Hospital and Health Network, Pennsylvania,  
United States

St. Luke's Hospital and Health Network, Bethlehem,  
Pennsylvania, United States,

United States, Washington

University of Washington, Seattle Cancer Care Center  
United States, Washington

Seattle, Washington, United States, University of  
Washington, Seattle Cancer Care Center

United States, ColoradoSeattle, Washington, United  
States

University of Colorado, Anschutz Cancer Pavil-  
lionUnited States, Colorado

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United States, WashingtonUniversity of Washington,  
Seattle Cancer Care Center

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							University of Colorado, Anschutz Cancer, Aurora, Colorado, United States States
							University of Washington, Seattle Cancer Care Center Seattle, Washington, United States,United States, ColoradoUniversity of Colorado, Anschutz Cancer Pavilion
Progressive Met- NCT00496860 astatic Malignancies	ALT-801	1	2007	Completed	26	MD Anderson Cancer Center Orlando, Florida, United States H. Lee Moffitt Cancer Center & Research Institute United States;;University of Colorado, Anschutz Cancer PavillionAurora, Colorado, United States Tampa, Florida, United States, H. Lee Moffitt Cancer Center & Research InstituteAurora, Colorado, United States,United States,Florida Seattle Cancer Care Center United States,	





NCT01639885	Recurrent Ovarian Cancer	Interferon Alfa-2b <b>p53</b> SLP	1 2	2011	Completed	15	Leiden University Medical Center Leiden, Netherlands
NCT01670994	Relapsed or Refractory Multiple Myeloma	ALT-801	1 2	2012	Terminated	6	University of Iowa Hospitals, Iowa City, Iowa, United States
NCT01625260	Non-muscle Invasive Bladder Cancer	ALT-801 Gemcitabine	1 2	2012	Unknown	52	University of Alabama Comprehensive Cancer Center Birmingham, Alabama, United States University of California Davis Sacramento, California, United States UF Health Center at Orlando Health Orlando, Florida, United States University of Oklahoma Health Science Center Oklahoma City, Oklahoma, United States UPMC Cancer Center Pittsburgh, Pennsylvania, United States,
NCT03725436	Advanced Malignant Solid Neoplasm Anatomic Stage III Breast Cancer AJCC v8 Anatomic Stage IIIA Breast Cancer AJCC v8 Anatomic Stage IIIB Breast Cancer AJCC v8	MDM2/MDMX Inhibitor ALRN-6924 Paclitaxel	1	2019	Recruiting	45	M D Anderson Cancer Center Houston, Texas, United States,

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Anatomic Stage  
IIIC Breast Cancer AJCC v8  
Estrogen Receptor Positive  
HER2/Neu Negative  
Metastatic Malignant Solid Neoplasm  
Prognostic Stage  
III Breast Cancer AJCC v8  
Prognostic Stage  
IIIA Breast Cancer AJCC v8  
Prognostic Stage  
IIIB Breast Cancer AJCC v8  
Prognostic Stage  
IIIC Breast Cancer AJCC v8  
Recurrent Breast Carcinoma  
**TP53 wt Allele**  
Unresectable Malignant Solid Neoplasm

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NCT01326871	Transitional Cell Carcinoma of Bladder	Cisplatin Gemcitabine ALT-801	1	2011	Unknown	90	The University of Arizona Cancer Center Tucson, Arizona, United States,
	Urethra Cancer		2				UF Health Center at Orlando Health Orlando, Florida, United States, Martin Health System Stuart, Florida, United States, H. Lee Moffitt Cancer Center and Research Institute Tampa, Florida, United States,
	Ureter Cancer						Emory University Atlanta, Georgia, United States,
	<b>Malignant Tu- mor of Renal Pelvis</b>						Robert Lurie Comprehensive Cancer Center of North- western University Chicago, Illinois, United States,
							University of Iowa Hospitals and Clinics Iowa City, Iowa, United States,
							University of Kansas Cancer Center Fairway, Kansas, United States,
							Karmanos Cancer Center Detroit, Michigan, United States,
							University of Minnesota Minneapolis, Minnesota, United States,
							Washington University St. Louis, Missouri, United States,
							Levine Cancer Institute Charlotte, North Carolina, United States,

								University of Oklahoma Health Science Center Oklahoma City, Oklahoma, United States,
								St. Luke's Hospital and Health Network Easton, Pennsylvania, United States,
								Thomas Jefferson University Hospital Philadelphia, Pennsylvania, United States,
								UPMC Cancer Center Pittsburgh, Pennsylvania, United States,
NCT03113487	Recurrent Platinum-Resistant Fallopian Tube Carcinoma Recurrent Platinum-Resistant Ovarian Carcinoma Recurrent Platinum-Resistant Primary Peritoneal Carcinoma	Modified Vaccinia Virus Ankara Vaccine Expressing p53 Pembrolizumab	2	2018	Recruiting	28		United States, California City of Hope Medical Center Duarte, California, United States,