Oncology Research and Treatment

Review Article

Oncol Res Treat
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Supplementary Tables

Supplementary table 1. Checkpoint inhibitors for use or in active development in lymphoma

Drug (generic name, product name)	target	type	Comments	FDA-approval	EMA-approval	Manufacturer
Urelumab	CD137/4-1BB	IgG4	Combination with Nivolumab			Bristol Myers Squibb
Utomilumab (PF-05082566)(1)	CD137/4-1BB	IgG2	Combination data with Rituximab			Pfizer
SEA-CD40	CD40	Sugar-engineered non-fucosylated antibody	Safety Study including lymphoma patients (NCT02376699)			Seatle Genetics
Hu5F9-G4	CD47	Humanized 5F9 mAb; IgG4	In combination with Rituximab in r/r B-NHL (NCT02953509)			Forty Seven Inc.
TTI-621	CD47	SIRP∂Fc recombinant Fusion protein	Intratumoral treatment of r/r MF (NCT02890368)			Trillium Pharmaceuticals
Ipilimumab (Yervoy)	CTLA-4	Human IgG1	First evaluated in relapsed lymphoma, 11% responses. Combination trials with Nivolumab under way.	Malignant Melanoma	Malignant Melanoma	Bristol Myers Squibb
Tremelimumab (CP-675)	CTLA-4	Fully human IgG2	Trial active to combine with MEDI4736 or AZD9150 in DLBCL (NCT02549651)			Medimmune/AstraZeneca
GWN323	GITR	Human IgG1	Phase I/Ib as single agent or with PDR001 in lymphoma (NCT02740270)			Novartis
MEDI-570	ICOS agonist		r/r pT-NHL or AILD (NCT02520791)			Medimmune/AstraZeneca
Epacadostat (INCB0244360)	IDO1	Small molecule	Interesting data in NSCLC, trials in lymphoma would be interesting			Incyte
Lirilumab (IPH2102/BMS986-015)	KIR	Fully humanized mAb	In MM within combination			BMS/Innate Pharma
IPH4102	KIR3DL2 agnoist		Study in In CTCL (NCT02593045)			Innate Pharma
BMS-986016	LAG-3	mAb	Combination with Nivolumab (NCT02061761)			Bristol Myers Squibb
MEDI6469	OX40		Combination with chemotherapy in first line DLBCL ongoing			
MEDI0680 (AMP-514)	PD-1	Humanized IgG4	MEDI-551 plus MEDI0680 in r/r aggressive Lymphoma (NCT02271945)			MedImmune/AstraZeneca

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Nivolumab (BMS-936558, Opdivo)	PD-1	Fully human IgG4 mAb (whole antibody)	> 40 trials in lymphoma (HD and NHL)	Classical Hodgkin lymphoma Advanced-stage RCC Metastatic NSCLC Malignant Melanoma	Malignant Melanoma, NSCLC, Renal Cell Carcinoma, Classical Hodgkin lymphoma	Bristol Myers Squibb
PDR001	PD-1	Humanized IgG4	s. above with GWN323 or with NIR178 in NHL (NCT03207867)			Novartis
Pembrolizumab (MK-3475) labbrolizumab, Keytruda)	PD-1	Humanized IgG4 mAb / whole antibody)	> 40 trials in lymphoma (HD and NHL)	Metastatic head and neck Malignant Melanoma Metastatic NSCLS	Malignant Melanoma, NSCLC, Urothelial Cancer	Merck
Atezolizumab (RG7446, MPDL3280A Tecentriq)	PD-L1	Fully humanized IgG1	10 trials active in lymphoma	Progressive locally advanced or metastatic urothelial carcinoma	none	Genentech/Roche
Avelumab (MSB0010718C)	PD-L1	Fully human IgG1	5 trials active in lymphoma	Merkel Cell carcinoma		Pfizer/Merck
BMS-936559 (MDX-1105)	PD-L1	Human mAb	Safety study in hem malignancies (NCT01452334)			Bristol Myers Squibb
Durvalumab (MEDI4736)	PD-L1	Fully human IgG1	Ongoing trial in lymphoma and CLL			MedImmune/AstraZeneca
MIW815	STING agonist		Single agent or in combination with PDR001 (NCT03172936)			Aduro Biotech
Pidilizumab	unknown	Humanized (from mouse) IgG1 mAb	Thought to be an PD-1-inhibitors, however mode of action now considered to be different. Results in DLBCL and FL promising, needs further clarification(2, 3)			Medivation/CureTech

Bold: approved drugs.

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Supplementary table 2. Overview of important clinical results

Disease	Drug	Phase	Dose used	Patients, n	ORR	CR	PFS	OS	NCT / Reference
CLL	Nivolumab (plus Ibrutinib)	II	N: 3mg/kg i.v. q 2 w, I: 420mg/d	5 r/r CLL 4 RT 3 CLL in PR after 9 mo of I	r/r CLL: 60% RT: 50%	CLL in PR: no CR	n.a.	n.a.	NCT02420912; [4]
CLL	Pembrolizumab	II	P: 200g i.v. q 3 w	25 (16 CLL, 9 Richter's syndrome)	CLL: 0% RT: 44%	CLL: 0% RT: 11%	n.a.	CLL: 59% @6mo RT: 73% @ 6mo	NCT02332980; [5]
CTCL	Pembrolizumab	II	2 mg/kg q 3 w up to 2 y	SS 18, MF 6	SS 33%, MF 50%	SS 0%, MF 33%	69% @ 12 m		NCT02243579 ; [6]
DLBCL	Nivolumab	Ib	1 or 3mg/kg w 1 and 4, then q2 w	11	36%	18%	Median 7 w		NCT01592370; [7]
DLBCL, post auto SCT consolidation	Pidilizumab	II	1.5mg/kg every 6 w for 3 cycles	66	51% (improvement of response)	34% (reversion to CR)	72% @ 16m		NCT00532259 ; [2]
FL	Nivolumab	Ib	1 or 3mg/kg w 1 and 4, then q2 w	10	40%	10%	Median n.r.		NCT01592370; [7]
FL	Pidilizumab	II	P 3mg/kg i.fv. q 4 we for max of 12, R 375mg/m2 q w for 4 doses	29 eligible	66%	52%	18.8 m		NCT00904722; [3]
MCL	Nivolumab	Ib	1 or 3mg/kg w 1 and 4, then q2 w	4	0%	n.a.	n.a.		NCT01592370; [7]
MF	Nivolumab	Ib	1 or 3mg/kg w 1 and 4, then q2 w	13	15%	0%			NCT01592370; [7]
PMBCL	Pembrolizumab	Ib	10mg/kg q 2 w (11), 200mg q 3 w	17	41%	12%	@ 11.3 m n.r.		NCT01592370; [7]
pTCL	Nivolumab	Ib	1 or 3mg/kg w 1 and 4, then q2 w	5	40%	0%			NCT01592370; [7]
Various: B-NHL	Nivolumab and Ipilimumab	I	N 3 mg/kg, I 1 mg/kg every 3 w for 4 doses, then N q 3w	15	20%	0%	1.5m		NCT01592370, [8]
Various: FL, DLBCL, MCL	Ipilimumab	I	3mg/kg initial and 1 or 3mg/kg monthly	18 (14 FL, 1 DLBCL, 1 MCL)	11%	5.5%	n.a.	n.a.	NCT00089076, [9]