

Development Pipeline Progress Status

November 1, 2019

Plan of submissions in Japan

OPDIVO
M=Mono
C=Combo

		Oncology	Non-Oncology
Onoact 〔Tachyarrhythmia upon sepsis〕 Aug 2019		OPDIVO 〔1L-RCC〕 with cabozantinib (C)	
ONO-2370 〔Parkinson's disease〕 Feb 2019	ONO-5704 〔Osteoarthritis〕	OPDIVO 〔1L-Gastric cancer〕 with Chemo (C)	OPDIVO 〔Adjuvant-Esophageal cancer〕 (M)
Coralan 〔CHF〕 Dec 2018	BRAFTOVI/MEKTOVI 〔BRAF mutated CRC〕	OPDIVO 〔1L-Gastric cancer〕 with YERVOY and with Chemo (C)	OPDIVO 〔1L-Malignant pleural mesothelioma〕 with YERVOY (C)
ONO-4059 〔PCNSL〕 Aug 2019	ONO-4059 〔WM/LPL〕	OPDIVO 〔Adjuvant-Urothelial cancer〕 (M)	OPDIVO 〔1L-Esophageal cancer〕 with YERVOY and with Chemo (C)
OPDIVO 〔2L-Esophageal cancer〕 (M) May 2019	OPDIVO 〔1L-NSCLC〕 with YERVOY (C)	OPDIVO 〔2L-Ovarian cancer〕 (M)	OPDIVO 〔Neoadjuvant-NSCLC〕 with YERVOY and with Chemo (C)
OPDIVO 〔MSI-High CRC〕 (M) Mar 2019	OPDIVO 〔480mg/Q4W〕 (M)	Kyprolis 〔Multiple myeloma〕 with DARZALEX	OPDIVO 〔1L-Head and neck cancer〕 with YERVOY (C)
ONO-7643 〔Cancer cachexia〕 Nov 2018	OPDIVO 〔MSI-High CRC〕 with YERVOY (C)	OPDIVO 〔1L-NSCLC〕 with YERVOY and Chemo (C)	OPDIVO 〔Adjuvant-Gastric cancer〕 with Chemo (C)
		OPDIVO 〔1L-NSCLC〕 with Chemo and AVASTIN (C)	OPDIVO 〔1L-Urothelial cancer〕 with YERVOY and with Chemo (C)
FY2018(2H)~2019(1H) (results)	FY2019 (2H)	FY2020 (1H)	FY2020 (2H)

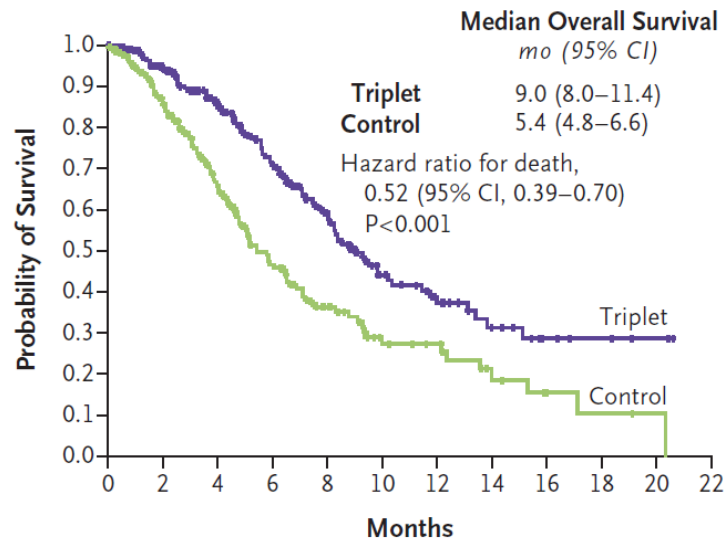
October 31 2019

BRAFTOVI/MEKTOVI - BRAF mutated CRC

BEACON CRC

Patients	Previously treated BRAF mutated mCRC
Regimen	<ul style="list-style-type: none"> ● Encorafenib 300mgQD + Binimetinib 45mgBID + Cetuximab ● Encorafenib 300mgQD + Cetuximab ● irinotetecan or FOLFIRI + Cetuximab
Endpoint	Primary : OS, ORR

A Overall Survival, Triplet Regimen vs. Control



No. at Risk	0	2	4	6	8	10	12	14	16	18	20	22
Triplet	224	186	141	103	69	37	24	14	6	4	2	0
Control	221	158	102	60	34	18	15	7	4	2	1	0

Table 2. Tumor Response in Patients with Metastatic Colorectal Cancer with the BRAF V600E Mutation.*

Variable	Triplet Regimen (N=111)	Doublet Regimen (N=113)	Control (N=107)
Objective response			
Patients with a complete or partial response — no. (%)	29 (26)	23 (20)	2 (2)
95% CI	18–35	13–29	<1–7
P value vs. control	<0.001	<0.001	
Best overall response — no. (%)			
Complete response	4 (4)	6 (5)	0
Partial response	25 (23)	17 (15)	2 (2)
Stable disease†	47 (42)	61 (54)	31 (29)
Progressive disease	11 (10)	8 (7)	36 (34)
Could not be evaluated according to RECIST‡	24 (22)	21 (19)	38 (36)
Clinical progression or discontinuation because of adverse event§	15 (14)	19 (17)	17 (16)
Insufficient data to assess response¶	9 (8)	2 (2)	21 (20)
Patients with duration of response ≥6 mo — no./total no. of patients with a response (%)	7/29 (24)	10/23 (43)	1/2 (50)
Patients with ongoing response and <6 mo follow-up — no./total no. of patients with a response (%)	4/29 (14)	1/23 (4)	0

S. Kopetz et al. N ENG J MED Sep 30, 2019

OPDIVO·YERVOY MSI-High CRC CA209142 (Phase II)

Patients	Previously treated MSI-High or dMMR mCRC
Regimen	<ul style="list-style-type: none"> ● Nivo 3 mg/kg Q2W ● Nivo 3 mg/kgQ3W + Ipi 1 mg/kgQ3W four doses followed by Nivo 3 mg/kgQ2W
Endpoint	Primary : ORR, Exploratory : PFS and OS etc.

Endpoints	Nivo + Ipi	Nivo
ORR	54.6%	31.1%
PFS 12m	71%	50%
OS 12m	85%	73%

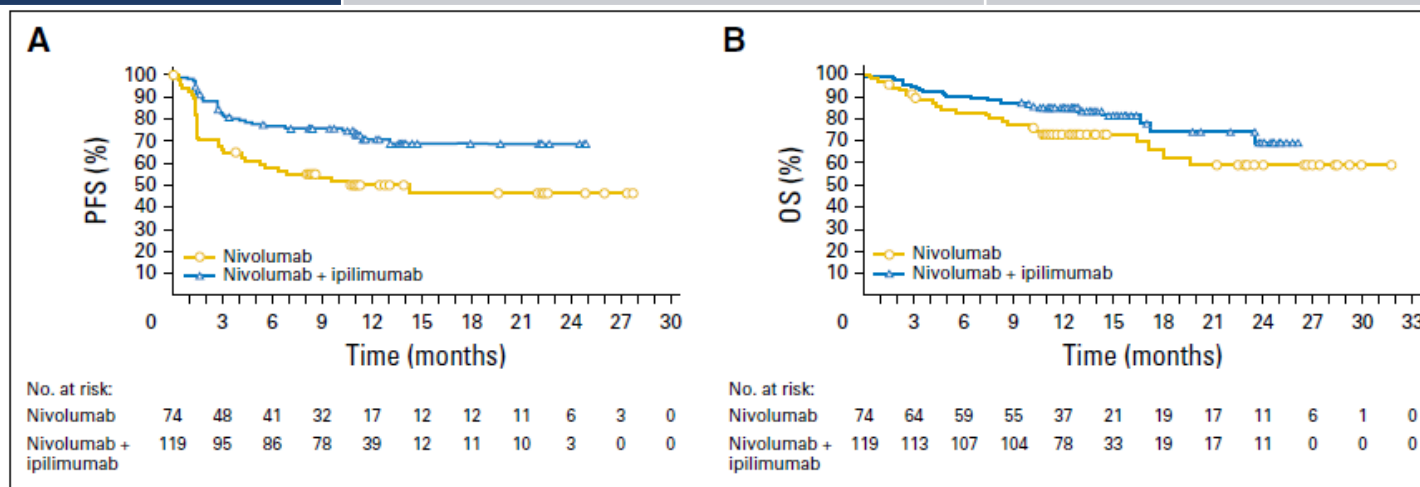


Fig 3. Kaplan-Meier plots of (A) progression-free survival (PFS) per investigator assessment and (B) overall survival (OS) in patients treated with nivolumab plus ipilimumab in the analyses presented herein or nivolumab in the monotherapy cohort of CheckMate-142 from an analysis that had a similar median follow-up (potential time on study from first dose to data cutoff: 13.4 months).¹¹

Overman MJ et al. J Clin Oncol, Jan 20 2018
Overman MJ et al. Lancet Oncol, July 19, 2017

Other Studies

【ONO-4538-77 / CA2099LA】

Patients	1L NSCLC
Regimen	<ul style="list-style-type: none">● Nivo 360mgQ3W + Ipi 1mg/kgQ6W + two cycles of chemotherapy● chemotherapy : four cycles followed by optional maintenance therapy
Endpoint	Primary : OS Secondary : PFS, ORR etc.

The trial met primary its endpoint at interim analysis

【ATTRACTION-5 / ONO-4538-38 / CA209844】

Patients	Resected pStage III Gastric cancer
Regimen	<ul style="list-style-type: none">● Nivo 360mgQ3W (1-year) + S-1 (1-year) or CapeOX (6-month)● investigators' choice : S-1 (1-year) or CapeOX (6-month)
Endpoint	Primary : RFS Secondary : OS

Development Pipeline Progress Status

October 31, 2019

Development status of OPDIVO (1)

As of October 25, 2019

Target disease	JAPAN	US/EU	KR/TW
Melanoma (1 st)	Approved	Approved	Approved
Melanoma (Adjuvant Therapy)	Approved	Approved	Approved
Non-small cell lung cancer (2 nd ~)	Approved	Approved	Approved
Non-small cell lung cancer (1 st)	Ⅲ	Ⅲ(US) Filing(EU)	Ⅲ
Renal cell carcinoma (2 nd ~)	Approved	Approved	Approved
Renal cell carcinoma (1 st)	Approved	Approved	Approved
Hodgkin's lymphoma	Approved	Approved	Approved
Head and neck carcinoma	Approved	Approved	Approved
Gastric cancer	Approved	Ⅲ	Approved
Malignant pleural mesothelioma	Approved	Ⅲ	-
Colorectal cancer (MSI-H)	Filing	Approved (US) Ⅱ /Ⅲ(EU)	Approved(TW)
Esophageal cancer	Filing	Ⅲ	Ⅲ
Gastro-esophageal junction cancer and esophageal cancer	Ⅲ	Ⅲ	Ⅲ
Small cell lung cancer	Ⅲ	Approved (US) Ⅲ (EU)	Ⅲ
Hepatocellular carcinoma	Ⅲ	Approved (US) Ⅲ (EU)	Ⅲ(KR) Approved (TW)

Red: Update after May 2019

Development status of OPDIVO (2)

As of October 25, 2019

Target disease	JAPAN	US/EU	KR/TW
Glioblastoma	III	III	-
Urothelial cancer	III	Approved	Approved
Ovarian cancer	III	III	-
Bladder cancer	III	III	III
Cervix carcinoma, Uterine body cancer, Soft tissue sarcoma	II	-	-
Central nervous system lymphoma, Primary Testicular Lymphoma	II	II	-
Pancreatic cancer	II	II	II
Virus positive/negative solid carcinoma	I / II	I / II	I / II
Biliary tract cancer	I	-	-
Multiple myeloma	-	III	-
Diffuse large B cell lymphoma (Non-Hodgkin's lymphoma)	-	II	-
Follicular lymphoma (Non-Hodgkin's lymphoma)	-	II	-
Prostate cancer	-	II	-
Pancreatic cancer, Triple negative breast cancer	-	I / II	-
Blood cancer (T-cell lymphoma, Multiple myeloma, Chronic leukemia, etc.)	-	I	-
Chronic myeloid leukemia	-	I	-

Clinical trials in combination therapy

OPDIVO & other Immuno-Oncology compounds (1)

As of October 25, 2019

Product name (Generic name) Pharmacological action	Cancer type	Japan	US/EU	KR/TW
Yervoy Injection (Ipilimumab) Anti-CTLA-4 antibody	Melanoma	Approved	Approved	Approved
	Renal cell carcinoma	Approved	Approved	Approved
	Non-small cell lung cancer	III	III(US) Filing(EU)	III
	Small cell lung cancer	III	III	III
	Head and neck cancer	III	III	III
	Gastric cancer	III	III	III
	Malignant pleural mesothelioma	III	III	-
	Esophageal cancer	III	III	III
	Urothelial cancer	III	III	III
	Hepatocellular carcinoma	III	III	III
	Colorectal cancer (MSI-H)	III	Approved(US) II (EU)	Approved(TW)
	Ovarian cancer	-	I / II	-
	Virus positive/negative solid carcinoma	I / II	I / II	I / II

Red: Update after May 2019



Clinical trials in combination therapy

OPDIVO & other Immuno-Oncology compounds (2)

As of October 25, 2019

Development code (Generic name) Pharmacological action	Cancer type	Japan	US/EU	KR/TW
ONO-7701 (Linrodostat) IDO1 inhibitor	Bladder cancer	III	III	III
ONO-4687 (Cabiralizumab) Anti-CSF-1R antibody	Pancreatic cancer	II	II	II
ONO-4686 Anti-TIGIT antibody	Solid tumor	I / II	I / II	-
ONO-7807 Anti-TIM-3 antibody	Solid tumor	I / II	I / II	-
ONO-4482 (Relatlimab) Anti-LAG-3 antibody	Melanoma	I / II	II / III	-
ONO-4483 (Lirilumab) Anti-KIR antibody	Solid tumor	I	I / II	-
ONO-7475 Axl/Mer inhibitor	Solid tumor	I	-	-
ONO-7911 (Bempegaldesleukin) PEGylated IL-2	Solid tumor	I	-	-

Red: Update after May 2019

Development pipeline in Japan (Oncology, other than OPDIVO)

As of October 25, 2019

Product name/ Development code (Generic name)	Target indication	Pharmacological action
【Filing】		
ONO-7643 (Anamorelin)	Cancer cachexia (in all types of cancer)	Ghrelin mimetic
KYPROLIS	Multiple myeloma <Change in dosage and administration>	Proteasome inhibitor
ONO-4059 (Tirabrutinib)	Central nervous system lymphoma	Btk inhibitor
【Phase III】		
BRAFTOVI (Encorafenib)	Colorectal cancer	BRAF inhibitor
MEKTOVI (Binimetinib)	Colorectal cancer	MEK inhibitor
【Phase II】		
ONO-4059 (Tirabrutinib)	Primary macroglobulinemia, Lymphoplasmacytic lymphoma	Btk inhibitor
【Phase I】		
ONO-4578*	Solid tumor	PG receptor (EP4) antagonist
ONO-7705 (Selinexor)	Multiple myeloma, Non-Hodgkin's lymphoma	XPO1 inhibitor
ONO-7475*	Solid tumor	Axl / Mer inhibitor

*Combination with Opdivo.

Red: Update after May 2019

Development pipeline in Japan (Non-oncology) (1)

As of October 25, 2019

Product name/ Development code (Generic name)	Target indication	Pharmacological action
【Filing】		
ONO-2370 (Opicapone)	Parkinson's disease	Long acting COMT inhibitor
ONOACT	Tachyarrhythmia upon sepsis	β₁ blocker (short acting)

【Phase III】		
ORENCIA SC	Untreated rheumatoid arthritis	T-cell activation inhibitor
	Primary Sjögrens syndrome	
	Polymyositis/Dermatomyositis	
ONO-5704 · SI-613	Osteoarthritis	Hyaluronic acid-NSAID

Red: Update after May 2019

Development pipeline in Japan (Non-oncology) (2)

As of October 25, 2019

Product name/ Development code (Generic name)	Target indication	Pharmacological action
【Phase II/III】		
ONOACT	Tachyarrhythmia in low cardiac function <Pediatric>	β_1 blocker (short acting)
【Phase II】		
ONO-5704 · SI-613	Enthesopathy	Hyaluronic acid-NSAID
ONO-4059 (Tirabrutinib)	Pemphigus	Btk inhibitor
【Phase I】		
ONO-7269	Cerebral infarction	FXIa inhibitor
ONO-4685	Autoimmune disease	PD-1 × CD3 Bispecific antibody

Red: Update after May 2019

Global development projects (Other than OPDIVO)

As of October 25, 2019

Development code (Generic name)	Target indication	Pharmacological action	Area
【Phase III】			
ONO-7702 (Encorafenib)	Colorectal cancer	BRAF inhibitor	KR
	Melanoma		KR
ONO-7703 (Binimetinib)	Colorectal cancer	MEK inhibitor	KR
	Melanoma		KR
【Phase II】			
ONO-4059 (Tirabrutinib)	B cell lymphoma	Btk inhibitor	EU
	Sjögrens syndrome		US/EU
【Phase I / II】			
ONO-4578*	Solid tumor	PG receptor (EP4) antagonist	US/EU
【Phase I】			
ONO-4059 (Tirabrutinib)	B cell lymphoma	Btk inhibitor	US
ONO-7475	Acute leukemia	Axl / Mer inhibitor	US
ONO-5788	Acromegaly	Growth hormone secretion inhibitor	US
ONO-7684	Thrombosis	FXIa inhibitor	EU

*Combination with Opdivo.