innate pharma

CONFERENCE CALL

NOVEMBER 14, 2016

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SPEAKERS

Hervé
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CEO & Co-founder

Immunotech SA,
Beckman-Coulter

Nicolai
WAGTMANN
PhD,
Chief Scientific Officer

Novo Nordisk A/S

Pierre
DODION
MD, MBA,
Chief Medical Officer
ARIAD, Pfizer, Novartis, Aventis

Jan B.
VERMORKEN
MD, PhD,
Emeritus Professor of Oncology

University of Antwerp, Belgium

JAN B. VERMORKEN, MD, PHD

EMERITUS PROFESSOR OF ONCOLOGY - UNIVERSITY OF ANTWERP BELGIUM

- 1986: PhD in Medical Sciences from the Vrije Universiteit in Amsterdam
- Medical Oncologist since 1992
- 1997-2009: Professor of Oncology at the University of Antwerp and head of the Department of Medical Oncology at the University Hospital Antwerp (Edegem, Belgium)
- Main fields of interest: gynecologic and head and neck cancer
  - > Founding chair of the Gynecologic Cancer InterGroup (1997-2003)
  - > Chaired both the Gynecologic Cancer Group (1983-1989) and Head and Neck Cancer Group (2006-2009) of the European Organization for the Research and Treatment of Cancer (EORTC)
- Member of various scientific societies and of several editorial boards of International journals
  - > 2009-2014: Editor-in-Chief of Annals of Oncology
  - > Editor of the head and neck cancer section of The Oncologist and Frontiers in Oncology

INTRODUCTION

HERVÉ BRAILLY

AGENDA

- Hervé Brailly
  - > Introduction: a key validation step for Innate Pharma
- Nicolai Wagtmann
  - > NK checkpoint inhibitors: a novel track in the I-O landscape
- Pierre Dodion
  - > Lirilumab in combination with nivolumab in Squamous Cell Carcinoma of the Head and Neck – summary of safety and efficacy data published at SITC 2016, November 12, 2016
  - > IPH4102 in Cutaneous T-Cell Lymphomas – summary of safety and efficacy data published at 3WCCL, October 28, 2016
- Hervé Brailly
  - > Perspectives
- Q&A

VALIDATION OF INNATE PHARMA'S NK POSITIONING
ENCOURAGING CLINICAL RESULTS FOR TWO FIRST-IN-CLASS ANTIBODIES

SITC 2016

NATIONAL HARBOR, MD
NOVEMBER 9-13, 2016

Preliminary efficacy from a phase 1/2 study of the natural killer cell–targeted antibody, lirilumab in combination with nivolumab in squamous cell carcinoma of the head and neck

Rom Leidner,[1] Hyunseok Kang,[2] Robert Haddad,[3] Neil H. Segal,[4] Lori J. Wirth,[5] Robert L. Ferris,[6] F. Stephen Hodi,[3] Rachel E. Sanborn,[1] Thomas F. Gajewski,[7] William Sharfman,[2] Dan McDonald,[8] Shivani Srivastava,[8] Xuemin Gu,[8] Penny Phillips,[8] Chaitali Passey,[8] Tanguy Y. Seiwert[7]

[1]Earle A. Chiles Research Institute, Providence Cancer Center, Portland, OR, USA; [2]The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA; [3]Dana-Farber Cancer Institute, Boston, MA, USA; [4]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [5]Massachusetts General Hospital, Boston, MA, USA; [6]University of Pittsburgh, Pittsburgh, PA, USA; [7]University of Chicago Medical Center, Chicago, IL, USA; [8]Bristol-Myers Squibb, Princeton, NJ, USA

sitc
Society for Immunotherapy of Cancer

#SITC2016

FIH, OPEN LABEL, MULTICENTER PHASE I STUDY OF IPH4102, FIRST-IN-CLASS HUMANIZED ANTI-KIR3DL2 MAB, IN RELAPSED/REFRACTORY CTCL: **PRELIMINARY SAFETY AND CLINICAL ACTIVITY RESULTS**

M. Bagot[*1,7], P. Porcu[3], C. Ram-Wolff[1,7], M. Vermeer[4], M. Khodadoust[2], M. Duvic[5], S. Whittaker[6], S. Mathieu[1], M. Battistella[1], A. Marie-Cardine[1,7], A. Bensussan[1,7], H. Sicard[8], C. Paiva[8], K. Pilz[8] and Y. Kim[2]

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[2]*Stanford Cancer Institute - Palo Alto, CA 94304, USA*
[3]*Ohio State University – Columbus, OH, USA*
[4]*LUMC - Leiden, the Netherlands*
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[6]*Guy's and St Thomas' Hospital – London, UK*
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[8]*INNATE PHARMA - 13009 Marseille, France*

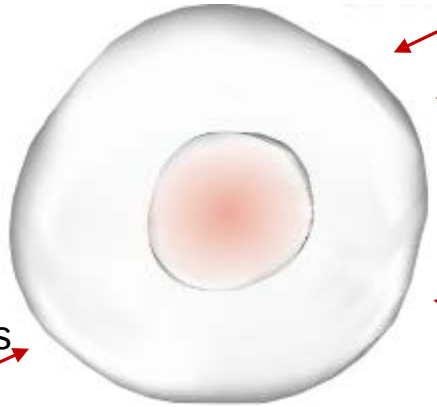
INNATE PHARMA'S UNIQUE VALUE PROPOSITION
NEW CLASS OF CHECKPOINT INHIBITORS TARGETING NK RECEPTORS

- IO development effort mostly target adaptive immunity
- Innate is a pioneer and at the forefront of targeting NK checkpoint inhibitors

Innate Pharma

Checkpoint inhibitors

Lirilumab | IPH/BMS
Monalizumab | IPH/AZN



Anti-CD137 | BMS, **Agonist mAB**

CD16-targeting bispecifics | Affimed
Bispecifics

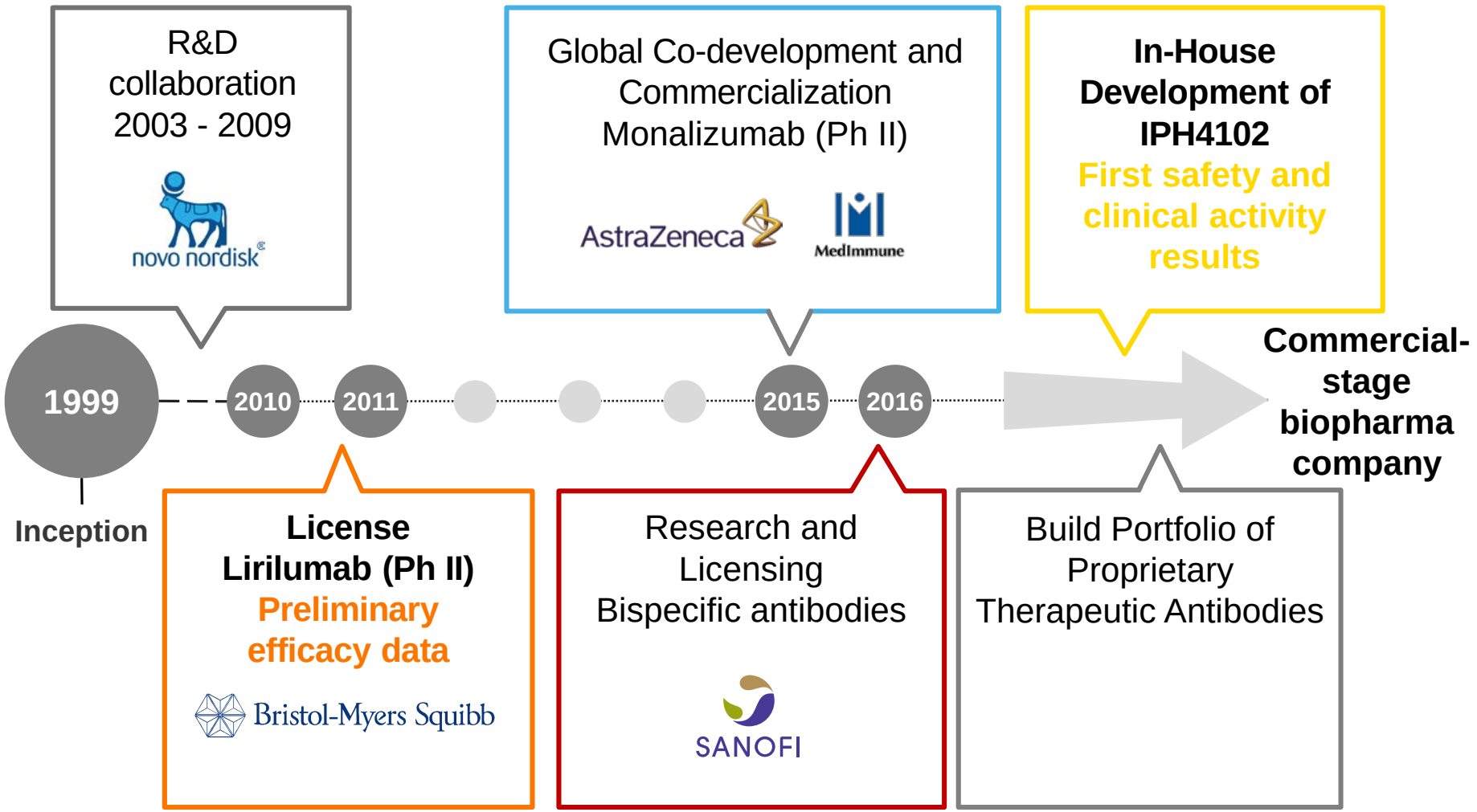
IL-12 - Celsion, **Cytokine**

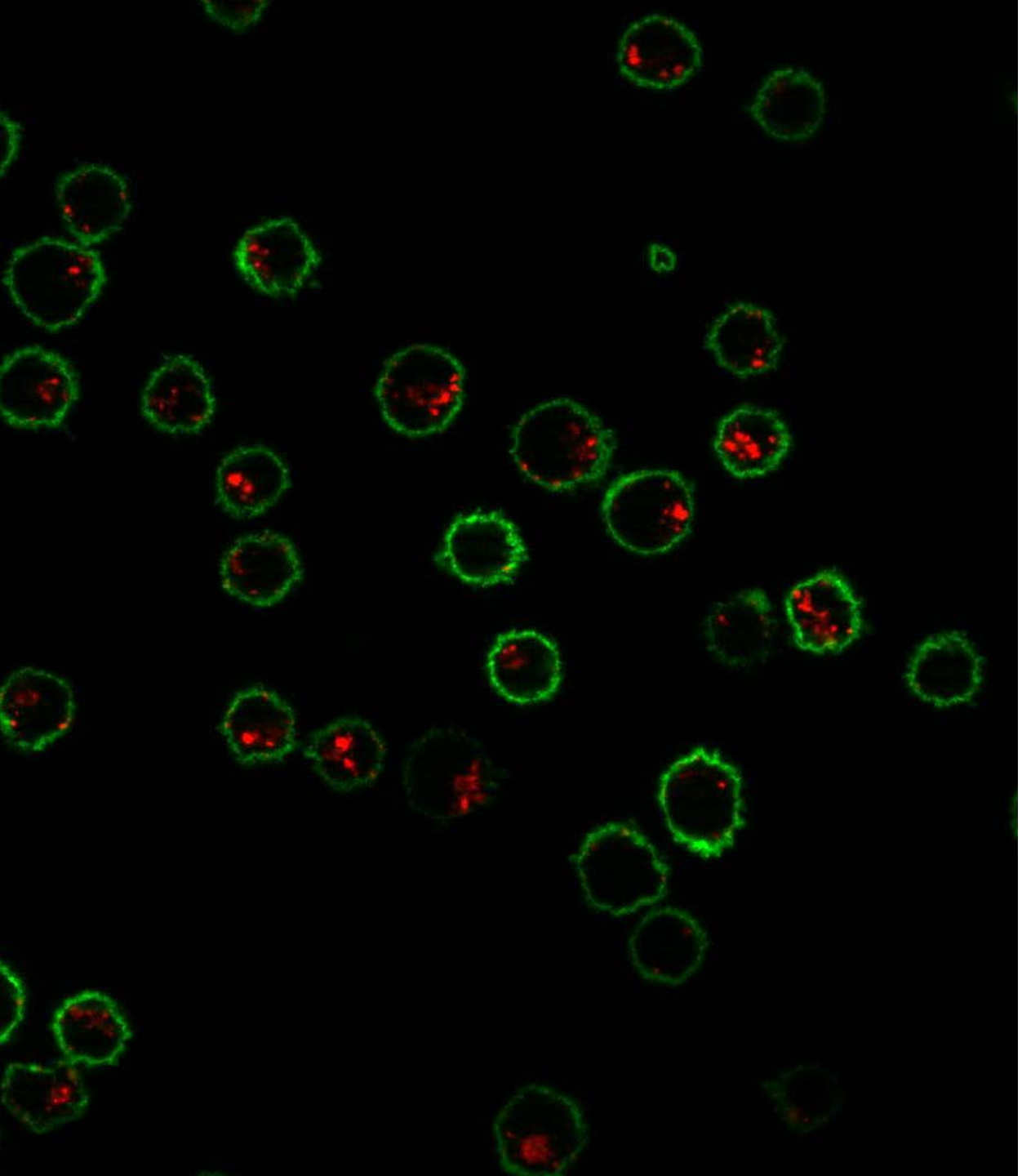
CEA-IL-2 | Roche,
Antibody-IL2 fusion proteins

CAR-NK cells | NantKwest, Celyad, Cytomx,
NK cell infusions | Celgene, Glycostem,
Cell therapy

NKp46-targeting bispecifics
Bispecific mAbs

STRATEGY
TO BECOME A COMMERCIAL STAGE BIOPHARMACEUTICAL COMPANY





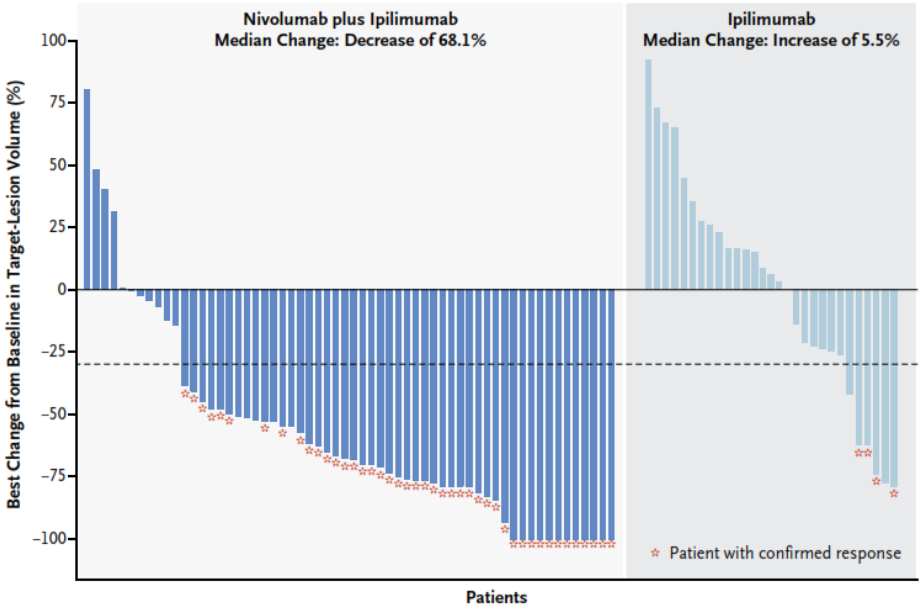
NK CHECKPOINT INHIBITORS: A NOVEL TRACK IN THE IMMUNO-ONCOLOGY LANDSCAPE

NICOLAI WAGTMANN

COMBINATIONS OF CHECKPOINT BLOCKERS
CAN LEAD TO DEEPER RESPONSES AND IMPROVED SURVIVAL

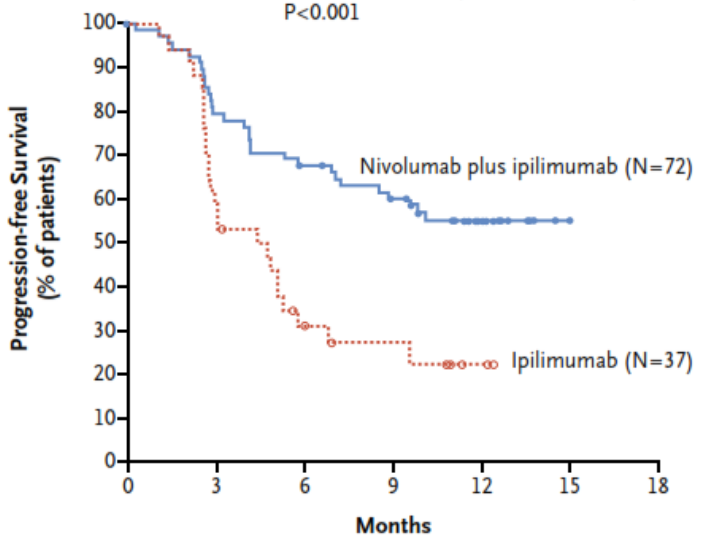
The NEW ENGLAND JOURNAL of MEDICINE

Nivolumab and Ipilimumab versus Ipilimumab in Untreated Melanoma



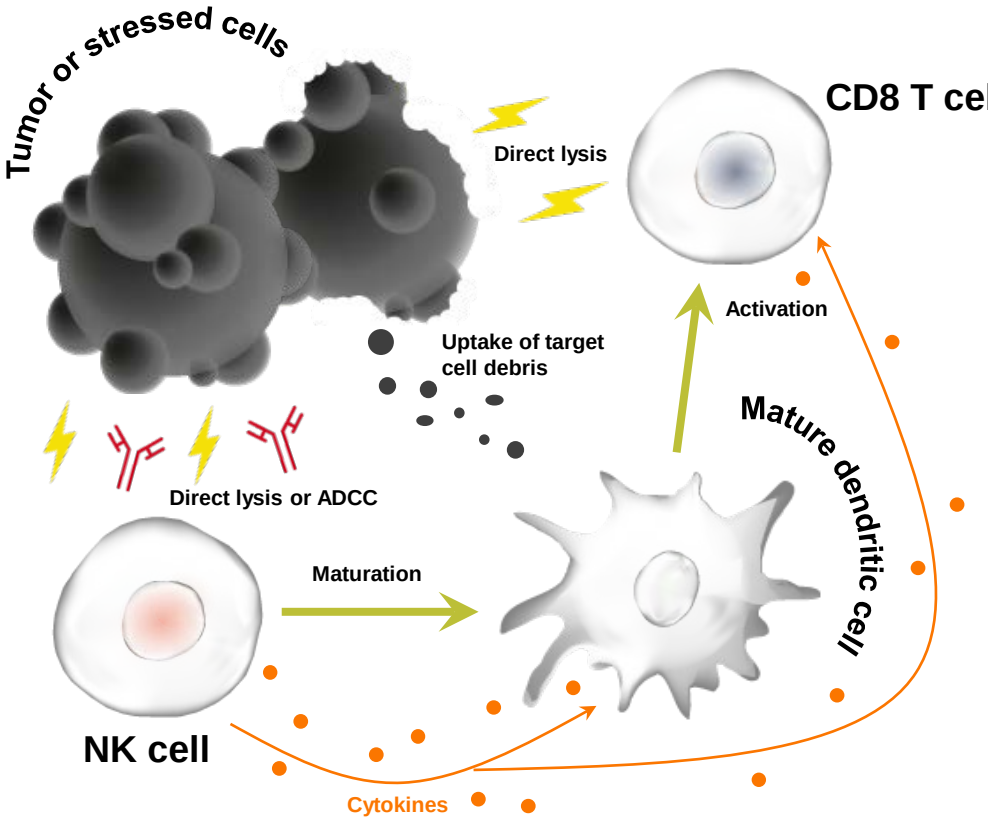
	Death or Disease Progression	Median Progression-free Survival
	no. of patients/total no.	*mo (95% CI)*
Nivolumab plus Ipilimumab	30/72	NR
Ipilimumab	25/37	4.4 (2.8–5.7)

Hazard ratio, 0.40 (95% CI, 0.23–0.68)
P<0.001



Postow et al. NEJM 2015

NATURAL KILLER (NK) CELLS IN IMMUNO-ONCOLOGY
DIRECT TUMOR KILLING AND HELP TO T CELLS

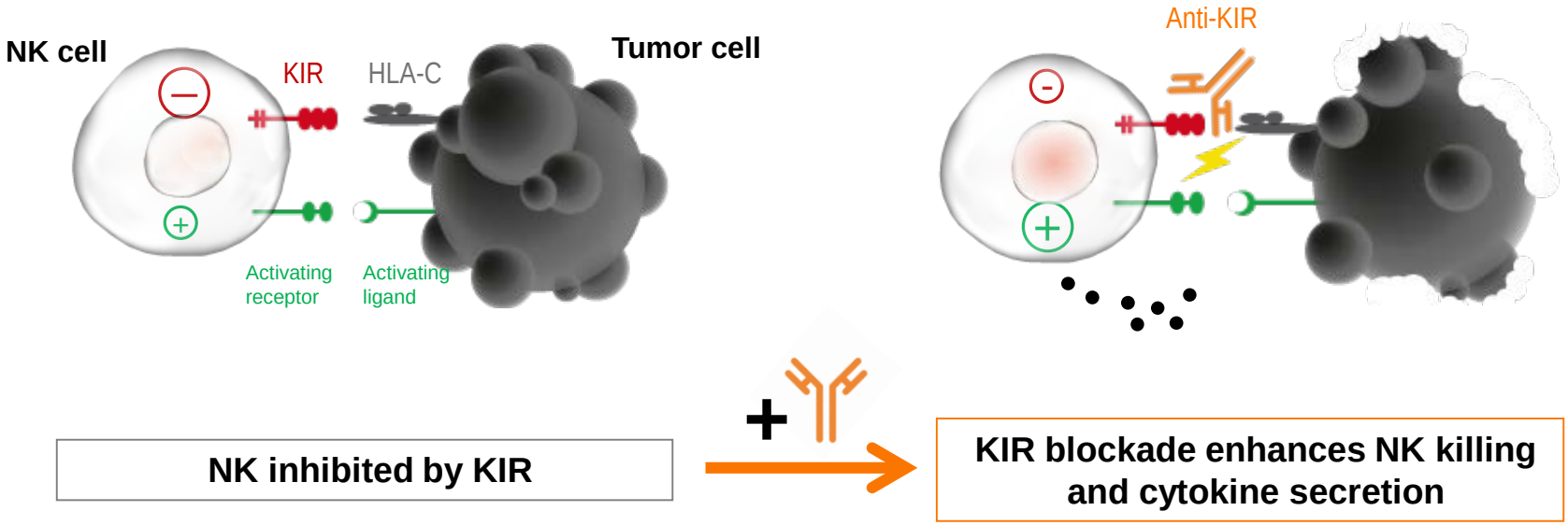


- Direct cytotoxicity:
  - > Kill tumors and stressed cells
  - > Triggered by conserved stress-antigens
- Promote T cell responses:
  - > Cytokine production: e.g. IFN-γ and IL-2
  - > Maturation of antigen presenting cells
  - > Promotion of immune memory

Adapted from Vivier et al., Nature Immunology 2008; Vivier et al., Science 2011

LIRILUMAB IS A FIRST-IN-CLASS KIR CHECKPOINT INHIBITOR
MECHANISM OF ACTION

- Fully human antibody (IgG4) blocking NK cell inhibitory receptor KIR2DL1,2,3
- Prevents interaction with HLA-C class I molecules to potentiate NK cell killing of tumor cells



- Lirilumab addresses distinct immune evasion mechanism
- Well tolerated in Phase I/II: opportunities for multiple combinations
- Potential for synergy with T cell checkpoint blocking antibodies

CLINICAL UPDATE

PIERRE DODION

SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK (SCCHN)

EPIDEMIOLOGY OF SCCHN

- SCCHN is the cancer with seventh highest prevalence globally
  - > About 3% of all cancers
  - > 600,000 cases diagnosed annually
  - > Higher incidence in men
- Vast majority are squamous cell carcinoma
- 75% of SCCHN are related to cigarette smoking and alcohol
  - > Particular case of HPV-related oropharyngeal cancer

- Standard treatment:
  - > Newly diagnosed, limited disease: radiation therapy, surgery
  - > Newly diagnosed, advanced disease: radiochemotherapy
  - > Patients with locoregionally recurrent and/or metastatic disease (“LRM SCCHN”)

WHO ARE THE PATIENTS WITH LRM SCCHN?

Local relapse

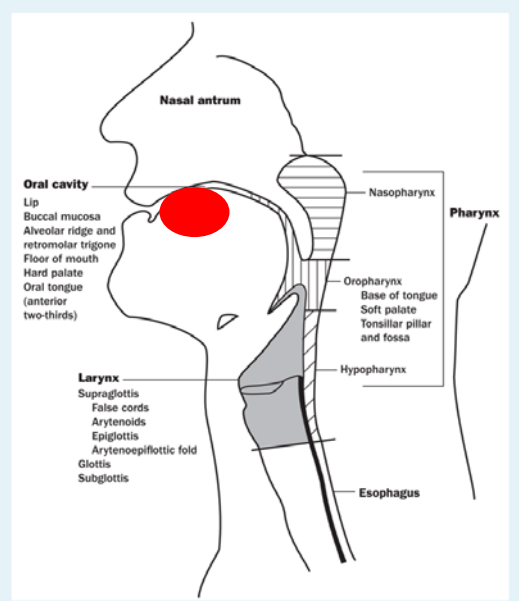
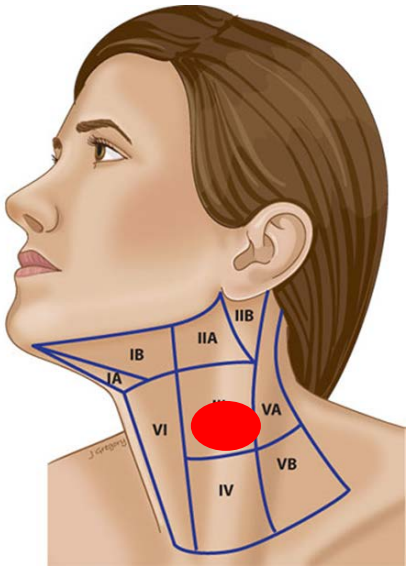


FIGURE 1: Anatomic sites and subsites of the head and neck. The approximate distribution of head and neck cancer is oral cavity, 44%; larynx, 31%; and pharynx, 25%.

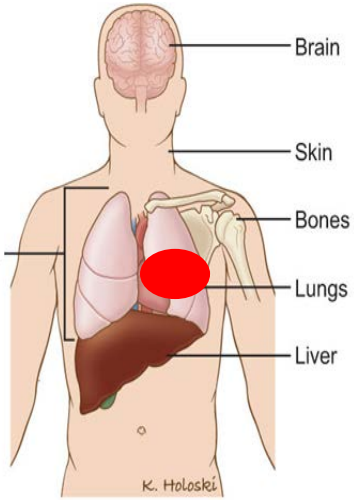
AND/ OR

Regional relapse



AND/ OR

Metastatic disease



For many years, systemic chemotherapy and cetuximab have been the only available options with poor outcome

CHEMOTHERAPY IN LRM SCCHN

First line

Aggressive approach: triplet chemotherapy

Platinum + 5-FU + cetuximab (EXTREME)

Docetaxel + cisplatin + 5-FU (TPF)

ORR	30-50%
CR	2-5%
PFS	4-6 months
OS	10 months

Non aggressive approach: doublet or single agent chemotherapy

Platinum ± fluorouracile, methotrexate, cetuximab, docetaxel,….

Second line

No standard treatment

Methotrexate, cetuximab, docetaxel, paclitaxel … (Cetuximab is the only approved drug in that setting)

ORR	< 15%
CR	0%
PFS	~ 2 months
OS	4-6 months

Best supportive care

Vermorken NEJM 2008 ; Sacco A. J Clin Oncol 2015; Vermorken J Clin Oncol 2007 ; Sacco A. J Clin Oncol 2015

ANTI-PD-1/PD-L1 IN SECOND LINE R/M SCCHN

- *Precaution: aim is to provide an overview of PD1/PDL1 inh, not to compare various drugs*
- *Trials are not identical in design (e.g. cutoff for PDL1 expression)*

	2nd line chemo [1]	**Nivolumab** Checkmate 141	**Pembrolizumab** Keynote 12 and 55		**Durvalumab**
ORR	**5.8%**	13.3%	18.0%	17.0%	13.8% [2]
CR	**0.8%**	2.5%	2.0%	0.0%	
PR	**5.0%**	10.8%	16.0%	17.0%	
Median PFS	**2.3 months**	2.0 months	2.1 months		
6-month PFS	**9.9%**	19.7%	24%		
Median OS	**5.1 months**	7.5 months	8.0 months		8.5 months
12-month OS	**16.6%**	36.0 %	38.0%		45%

[1] From Checkmate 141 study
[2] 18% in PDL1 high and 8% in PDL1 low

Ferris J Clin Oncol 2016; Seiwert Lancet Oncol 2016; Segal ESMO 2016 (abstract 949O)

ANTI-PD-1/PD-L1 IN SECOND LINE R/M SCCHN
REGULATORY STATUS

- Keytruda
  - > FDA: Accelerated approval granted for RM SCCHN with disease progression on or after platinum-containing chemotherapy.
  - > EMA: Under review

- Opdivo
  - > FDA: Approved for RM SCCHN with disease progression on or after a platinum-based therapy
  - > EMA: Under review

PHASE 1/2 ANTI-KIR IN COMBINATION WITH ANTI-PD-1

CA223-001 DATA

TRIAL CA223-001
ELIGIBILITY CRITERIA AND TREATMENT SCHEDULE

Eligibility criteria for the entire study:

- Advanced solid tumors; ≤ 5 lines of prior therapy; ≥ one in the escalation part
- ECOG PS ≤ 1

Eligibility criteria specific to the SCCHN cohort:

- Progression or recurrence within 6 months of platinum treatment (primary or LRM setting)
- Mandatory pre- and on- treatment biopsy in 15 patients

Treatment:

- Nivolumab 3.0 mg/kg q2w
- Lirilumab 0.1-0.3-1.0-3.0 mg/kg q4w in escalation part; 3.0 mg/kg in expansion cohorts
- Until progression, excessive toxicity, confirmed CR or max 24 months

TRIAL CA223-001: TREATMENT-RELATED ADVERSE EVENTS (TRAES) - ALL EXPANSION COHORTS COMBINED

Patients with TRAE, n (%)	All Patients (N = 159)	
	Any Grade	Grade 3/4
Any TRAE	114 (71.7)	24 (15.1)
TRAEs in > 10% of all patients		
Fatigue	33 (20.8)	0
Pruritus	30 (18.9)	0
Infusion-related reaction	28 (17.6)	0
Rash	26 (16.4)	0
TRAEs leading to discontinuation	12 (7.5)	4 (2.5)*
Leading to discontinuation in > 1 patient		
Pneumonitis	3 (1.9)	0
Diarrhea	2 (1.3)	0

***Grade 3/4 TRAEs leading to discontinuation were electrocardiogram QT prolonged (grade 3), hypopituitarism (grade 3), lipase increased (grade 3), and thrombocytopenia (grade 4).**

- No DLTs were reported; rash and infusion-related reactions were clinically manageable
- No treatment-related deaths were reported

Segal NH, et al. Ann Oncol. 2016;27: Abstract 1086P; Hodi FS, et al. Presented at: New Cancer Immunotherapy Agents in Development. Wed November 9, 2016

DEMOGRAPHICS OF PATIENTS WITH SCCHN

TREATED WITH LIRILUMAB + NIVOLUMAB (CA223-001) OR NIVOLUMAB MONOTHERAPY (CHECKMATE 141[1])

	Lirilumab + Nivolumab (n = 41)*	Nivolumab alone[1] (N = 240)
ECOG PS, n (%)**		
0	9 (22.0)	49 (20.4)
1	32 (78.0)	189 (78.8)
≥2	0	1 (0.4)
Tumor location, n (%)		
Oral cavity	23 (56.1)	108 (45.0)
Pharynx and/or oropharynx	14 (34.1)	92 (38.3)
Larynx	3 (7.3)	34 (14.2)
Other	1 (2.4)	6 (2.5)
Prior therapies, n (%)		
1	13 (31.7)	106 (44.2)
2	17 (41.5)	80 (33.3)
≥3	11 (26.8)	54 (22.5)
HPV-positive oropharynx, n (%)‡	8 (19.5)	63 (26.2)

*Of the 41 patients with SCCHN, 29 were evaluable for response. Majority of non-evaluable patients had not yet reached first on-study treatment assessment. 26 patients had post-baseline scans; 3 progressed prior to first scans.

** ECOG performance status was not reported in 1 patient in CheckMate 141.

‡ For CheckMate 141, HPV status according to p16 positivity.

1. *Ferris RL, et al. N Engl J Med. 2016 Oct 8 [Epub ahead of print]*

EFFICACY DATA IN CA223-001 AND CHECKMATE 141
IN EVALUABLE PATIENTS WITH SCCHN

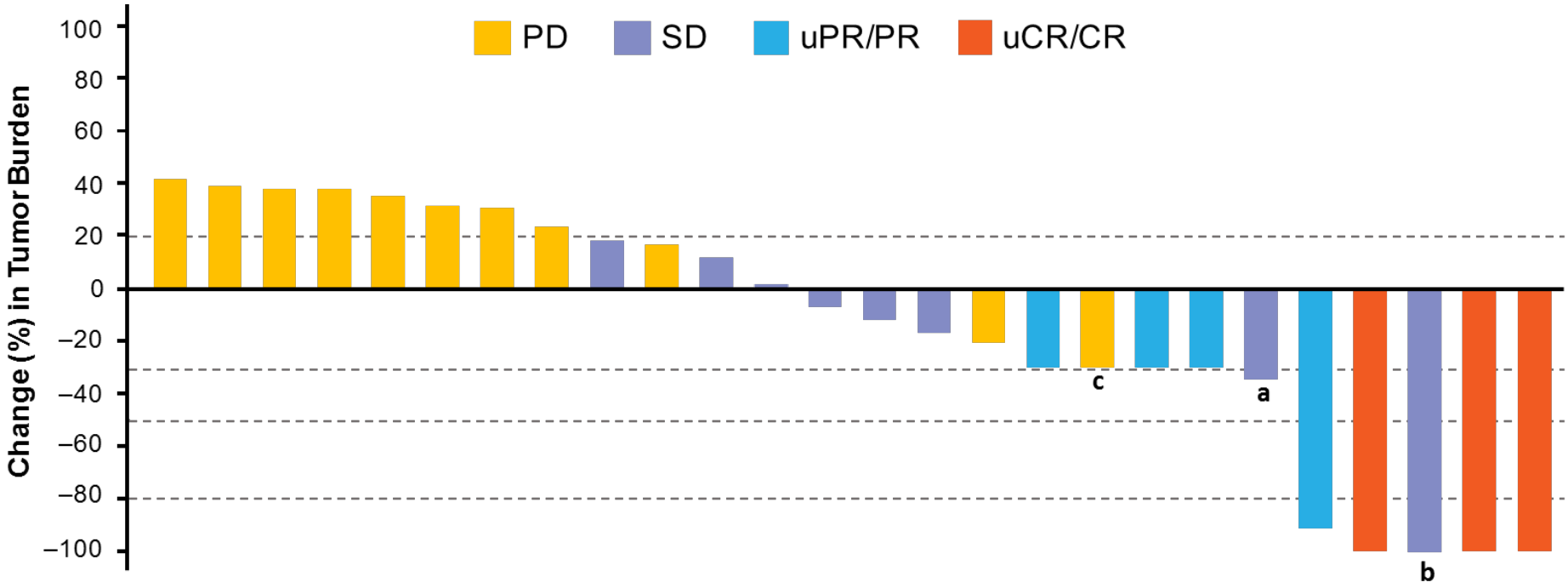
	Lirilumab + Nivolumab	Nivolumab alone[1]
ORR, n/N (%)	**7/29 (24.1)***	**32/240 (13.3)**
Complete response	3 (10.3)*	6 (2.5)
Partial response	4 (13.8)*	26 (10.8)
DCR, n/N (%)	15/29 (51.7)	NR
ORR by PD-L1 expression, n/N (%)†		
<1%	0/9 (0)	9/73 (12.3)
≥1%	7/17 (41.2)	15/88 (17.0)
≥5%	6/11 (54.5)	12/54 (22.2)
≥50%	4/7 (57.1)	7/19 (36.8)
Overall survival, % (95% CI)		
At 6 months	90‡	55.6 (48.9, 61.8)
At 12 months	60§	36.0 (28.5, 43.4)

* Includes unconfirmed responses.
† PD-L1 expression was not determined in 3 patients; none of these patients were responders.
‡Patients at risk, n = 15/41. §Patients at risk, n = 10/41.

1. ***Ferris RL, et al. N Engl J Med. 2016 Oct 8 [Epub ahead of print]***

PRELIMINARY MAXIMUM PERCENT REDUCTION IN TARGET LESIONS

IN EVALUABLE PATIENTS WITH SCCHN TREATED WITH LIRILUMAB + NIVOLUMAB (N = 26)*

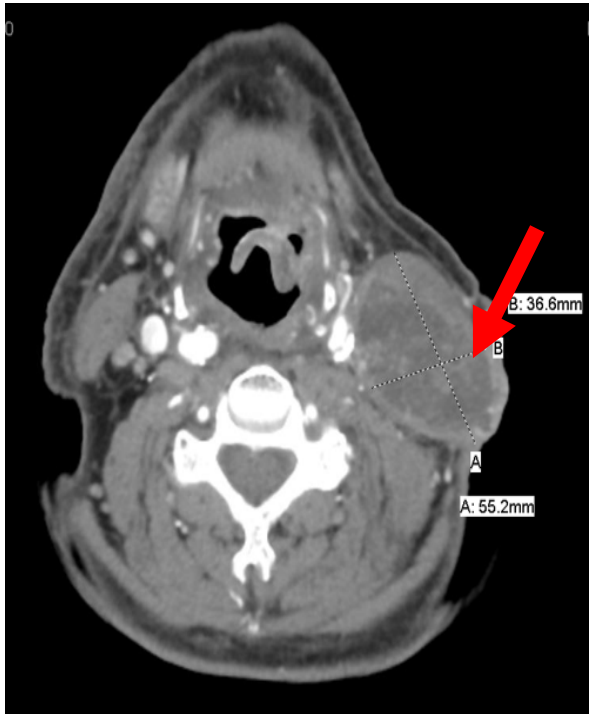


Of the seven patients with a response, none were HPV-positive oropharyngeal patients

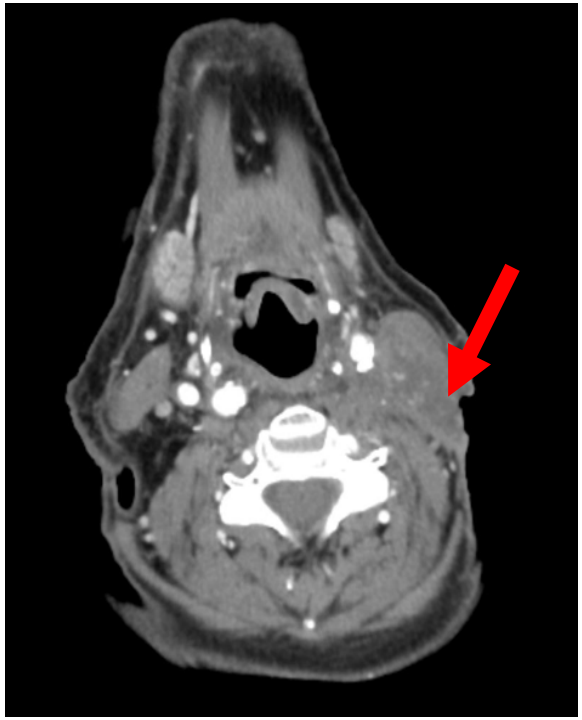
*26 of 29 evaluable patients had a post-baseline assessment.
[a] Patient with a 37% reduction in target lesion classified as SD.
[b] Patient with a 100% reduction in target lesion classified as SD.
[c] Patient with a 30% reduction in target lesion classified as PD.

67-YEAR-OLD MALE PATIENT
WITH HPV-NEGATIVE SCCHN OF LARYNX

19 JUN 2014: 36 mm

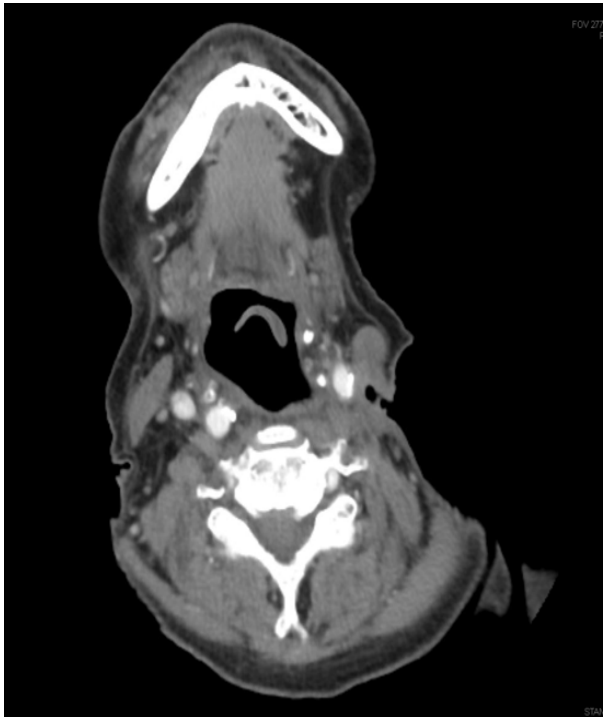


2 SEP 2014: 25 mm
4 doses of nivolumab
+ 2 doses of lirilumab



Overall tumor burden :
45% decrease by RECIST

6 JAN 2015: 0 mm
12 doses of nivolumab
+ 6 doses of lirilumab

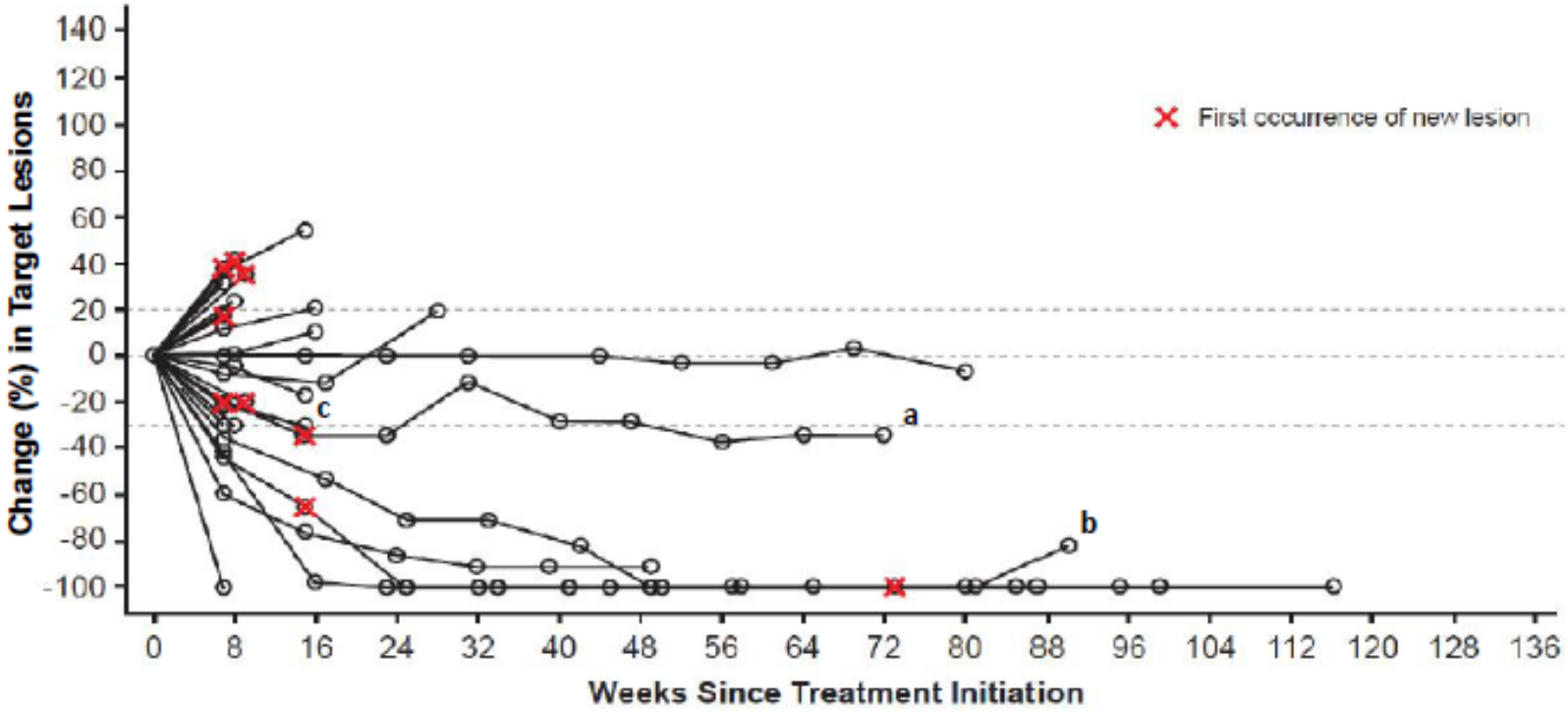


Overall tumor burden :
100% decrease of target lesions*

* Patient developed new lesions after 2nd cycle but continued in trial with resolution of target lesions

PRELIMINARY PERCENT CHANGE FROM BASELINE IN TARGET LESIONS OVER TIME

IN EVALUABLE PATIENTS WITH SCCHN TREATED WITH LIRILUMAB + NIVOLUMAB (N = 26)*



The median DOR was not reached

*26 of 29 evaluable patients had a post-baseline assessment.
[a] Patient with a 37% reduction in target lesion classified as SD.
[b] Patient with a 100% reduction in target lesion classified as SD.
[c] Patient with a 30% reduction in target lesion classified as PD.

LIRILUMAB + NIVOLUMAB IN SCCHN
CONCLUSIONS FROM PRELIMINARY DATA OF CA223-001

- This is the first report of efficacy with the anti-KIR agent lirilumab in combination with nivolumab
- **Potential for a differentiated profile in this patient population with enhanced clinical activity, particularly in inflamed tumors and with deep and durable responses observed in some patients**
- The combination of lirilumab and nivolumab achieved an **ORR of 24% in 29 evaluable patients**
  - > **41% in patients with inflamed tumors (>1% PD-L1 expression)**
- Encouraging early overall survival data
- No added toxicity over nivolumab monotherapy observed
- Further evaluation of the safety and efficacy of lirilumab + nivolumab is ongoing in a broad exploratory program
- **Offers the potential for a new generation of IO/IO combinations**

IPH4102 UPDATE

DATA FROM DOSE-ESCALATION PART OF PHASE I TRIAL
IPH4102 IS WELL TOLERATED

- Preliminary results reported at 3WCCL[2] in November 2016 on the first 7 dose levels (0.0001 to 1.5 mg/kg)
  - > 16 patients evaluable for safety and efficacy (13 SS, 2 MF and 1 $CD4^+$ CTCL)
  - > Elderly and heavily pretreated patients: median age of 71 years; 2 to 8 lines of prior systemic therapy

- **Good safety profile with no dose limiting toxicity reported**
  - > Majority of AEs typical for CTCL or reflects low grade infusion-related reactions
  - > Vast majority were grade 1-2; only one grade 3 and one grade 4
  - > Only 38% of the patients experienced a treatment related AE – none grade 3 or 4

- **Three additional dose-levels (3, 6 and 10 mg/kg) remain to be evaluated**

Bagot et al., 3WCCL poster 2016 ; 2. Third World Congress of Cutaneous Lymphoma; 3. Marie-Cardine et al., 3WCCL poster 2016

DATA FROM DOSE-ESCALATION PART OF PHASE I TRIAL IPH4102 SHOW ENCOURAGING PRELIMINARY EFFICACY

	Best global response – all patients	Sezary syndrome			
		Best global response	Best response In skin	Best response In blood	Best response In lymph nodes
	N=16	n=13	N=13	N=13	N=9
CR	0	0	2	3	0
PR	6	5	4	5	1
ORR	38%	38%	46%	62%	11%
Treatment duration (days) Median Min Max	 126+ 41+ 298+	 132+ 41+ 298+			

- **Results of exploratory endpoints such as pharmacodynamics in skin and blood are in line with clinical activity results[3]**

Bagot et al., 3WCCL poster 2016 ; 2. Third World Congress of Cutaneous Lymphoma; 3. Marie-Cardine et al., 3WCCL poster 2016

PRELIMINARY SAFETY AND EFFICACY DATA: CONCLUSIONS

- Preliminary safety and efficacy data from 16 patient with CTCL
- IPH4102 appears to be well tolerated, despite the fact that the patients were elderly and heavily pretreated
- Adverse events are typical for CTCL patients or reflect low grade infusion reactions
- Encouraging activity with a response rate of 38%
  - > All responses are ongoing
  - > Some complete responses in the skin and the blood
- The last 3 dose levels (3, 6 and 10 mg/kg) are being explored
- End of dose-escalation expected by Q2 2017

PERSPECTIVES

HERVÉ BRAILLY

KEY TAKE AWAY MESSAGES

- Encouraging clinical results for two of Innate's first-in-class antibodies
  - > Lirilumab + nivolumab: preliminary evidence of clinical benefit in patients with patients with advanced platinum refractory squamous cell carcinoma of the head and neck
  - > IPH4102: preliminary evidence of activity in CTLC
- Validates Innate's pioneer approach in innate immunity modulation and NK cell biology
- Supports our ambition to be at the forefront of developing novel combination immunotherapies

CLINICAL PROGRAM READ OUT
NEAR TERM NEWSFLOW

- **Monalizumab: Safety data of monalizumab as a single agent in ovarian cancer**
  EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics 2016 congress (29 November – 2 December, Munich)

- **Lirilumab: Data from in Phase Ib/II study in relapsed AML of lirilumab in combination with azacytidine**
  ASH Annual Meeting (December 3-6, San Diego, CA)

- **IPH4102: preliminary safety, exploratory and clinical activity results from 7 first dose levels**
  ASH Annual Meeting (December 3-6, San Diego, CA) – same data as 3WCCL

- **Lirilumab: topline data for lirilumab as a single-agent as a maintenance treatment in AML (EffiKIR)**
  Early 2017

APPENDIX

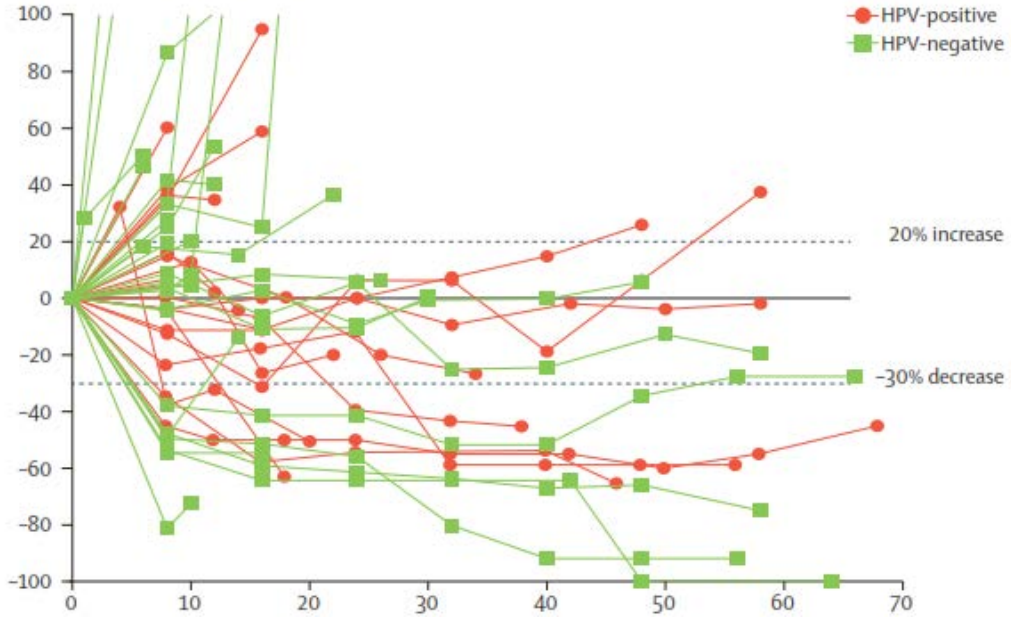
PEMBROLIZUMAB IN LRM SCCHN

- Keynote 12 study (NCT01848834): open-label, multicenter, phase 1b trial of patients with LRM SCCHN
  - > at least 1% of tumor cells or stroma that were PD-L1-positive by immunohistochemistry)
  - > pembrolizumab 10 mg/kg intravenously every 2 weeks
  - > Primary outcomes: safety and overall response rate (RECIST, version 1.1)
- Keynote 55 study (NCT02255097): open-label, multicenter nonrandomized phase 2 trial in LRM SSCHN resistant to platinum and cetuximab
  - > Pembrolizumab administered intravenously at a dose of 200 mg every 3 weeks
  - > Mandatory biopsy prior to treatment for evaluation of PD-L1
  - > Primary efficacy parameter: ORR (RECIST v1.1)
  - > Secondary efficacy end points: duration of response, ORR per modified RECIST v1.1, PFS, and OS

Seiwert et al. Lancet Oncol 2016;17:956-65; Bauml et al. J J Clin Oncol 34, 2016 (suppl; abstr 6011)

PEMBROLIZUMAB IN LRM SCCHN

Response category	N	%	95% CI
Overall - Complete - partial	8 1 7	18 2 16	8-32 <1-12 7-30
Stable disease	8	18	8-32
Progression	25	56	40-70

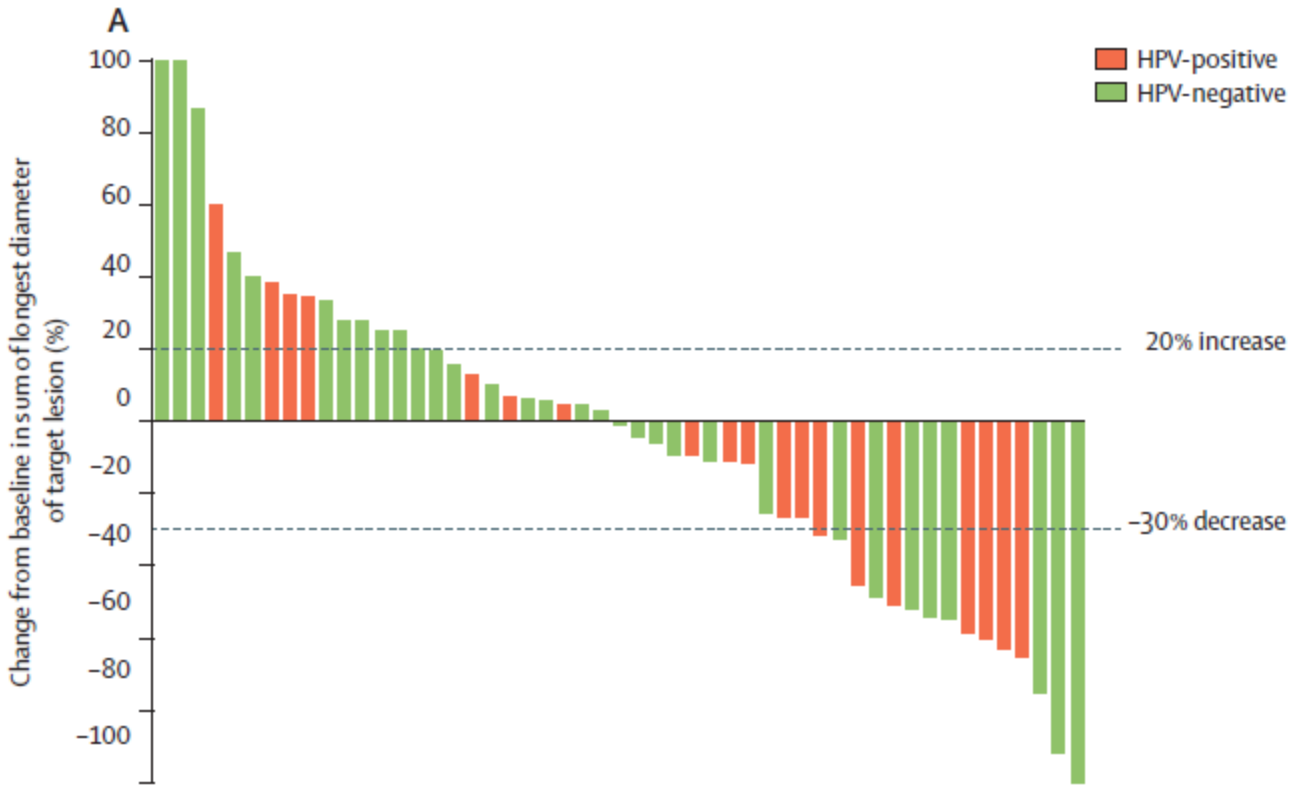


Some association with PDL1 expression but small sample size

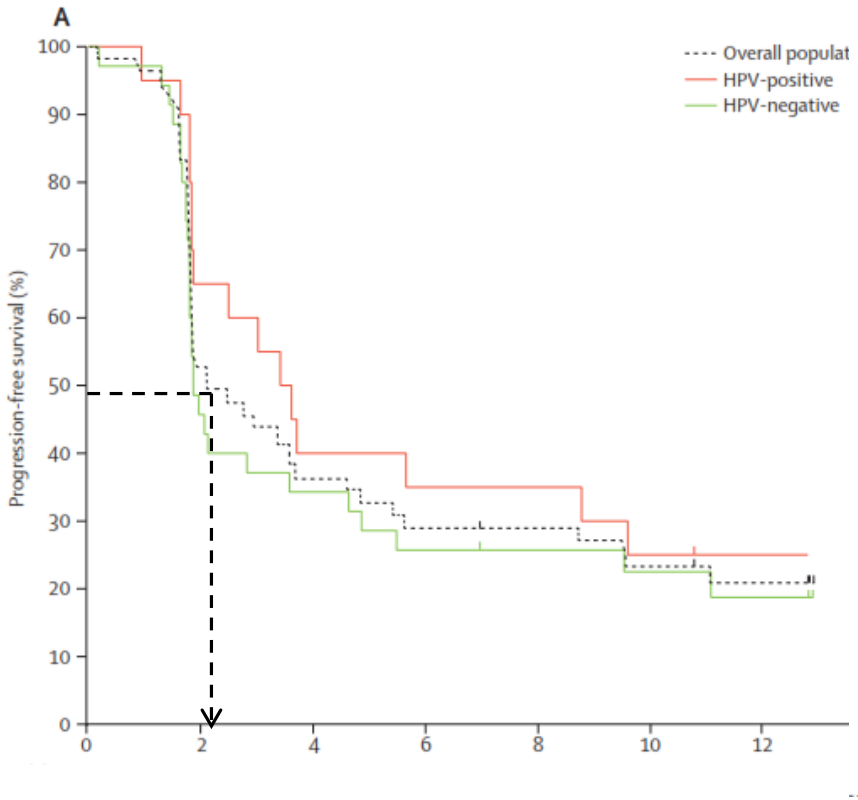
Seiwert et al. Lancet Oncol 2016;17:956-65

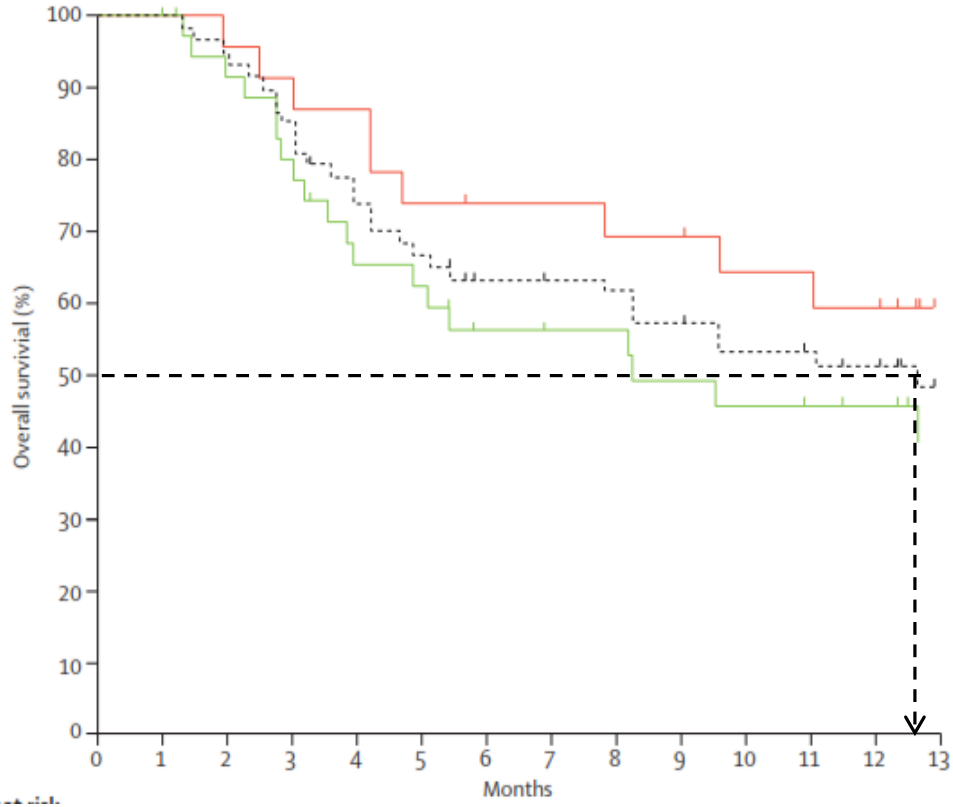
PEMBROLIZUMAB IN LRM SCCHN

WATERFALL PLOT



PEMBROLIZUMAB IN LRM SCCHN





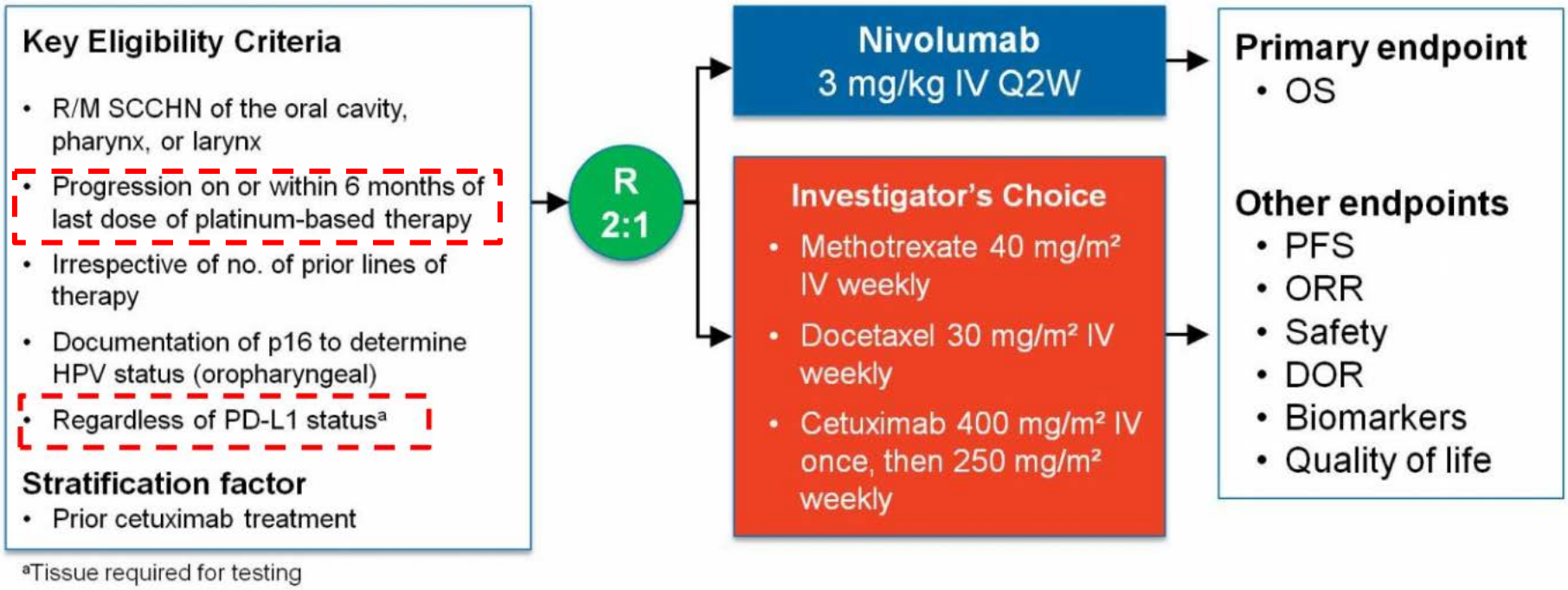
Med PFS = 2 months

Med OS = 13 months

Seiwert et al. Lancet Oncol 2016;17:956-65

NIVOLUMAB IN LRM SCCHN
CHECKMATE 141 STUDY DESIGN

Randomized, global, phase 3 trial of the efficacy and safety of nivolumab vs investigator's choice in patients with R/M SCCHN



[a]Tissue required for testing

DOR = duration of response; IV = intravenous; ORR = objective response rate; PFS = progression-free survival; Q2W = once every 2 weeks; R = randomized. Clinicaltrials.gov NCT02105636.

2016 ASCO Annual Meeting; Ferris et al, NEJM 2016

NIVOLUMAB IN LRM SCCHN

OS BY PDL1 EXPRESSION

PDL1 expression level	HR for death (95% CI)	Nivolumab		Standard therapy	
		N	Median survival (months)	N	Median survival (months)
All patients	0.69 (0.53-0.91)	240	7.5	121	5.1
≥ 1%	0.55 (0.36-0.83)	88	8.7	61	4.6
< 1%	0.89 (0.54-1.45)	73	5.7	38	5.8
≥ 5%	0.50 (0.30-0.83)	54	8.8	43	4.6
< 5%	0.81 (0.55-1.21)	107	7.0	56	5.1
≥ 10%	0.56 (0.31-1.01)	43	8.7	34	5.2
< 10%	0.73 (0.50-1.06)	118	7.2	65	4.6

NIVOLUMAB IN LRM SCCHN
OBJECTIVE RESPONSE RATE

	Nivolumab (n = 240)	Investigator's Choice (n = 121)
Objective response rate, n (%)	32 (13.3)	7 (5.8)
95% CI	9.3, 18.3	2.4, 11.6
Best overall response, n (%)		
Complete response	6 (2.5)	1 (0.8)
Partial response	26 (10.8)	6 (5.0)
Stable disease	55 (22.9)	43 (35.5)
Progressive disease	100 (41.7)	42 (34.7)
Not determined	53 (22.1)	29 (24.0)

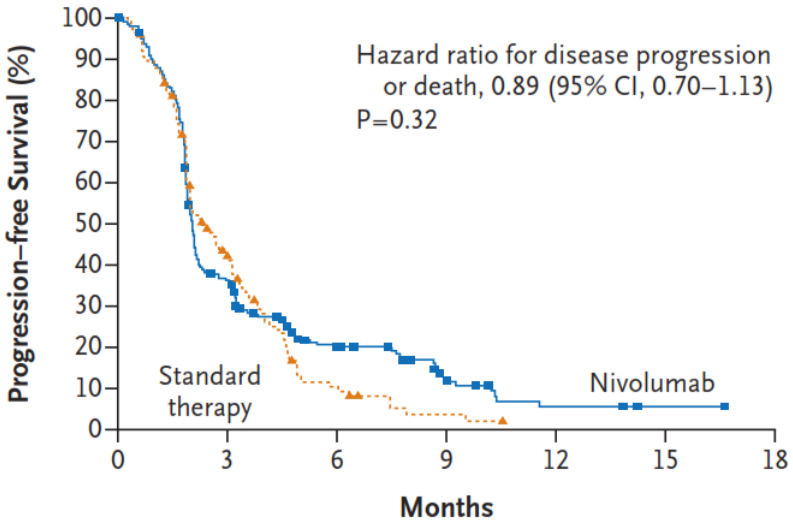
2016 ASCO Annual Meeting; Ferris et al, NEJM 2016

NIVOLUMAB IN LRM SCCHN

PROGRESSION FREE AND OVERALL SURVIVAL DATA

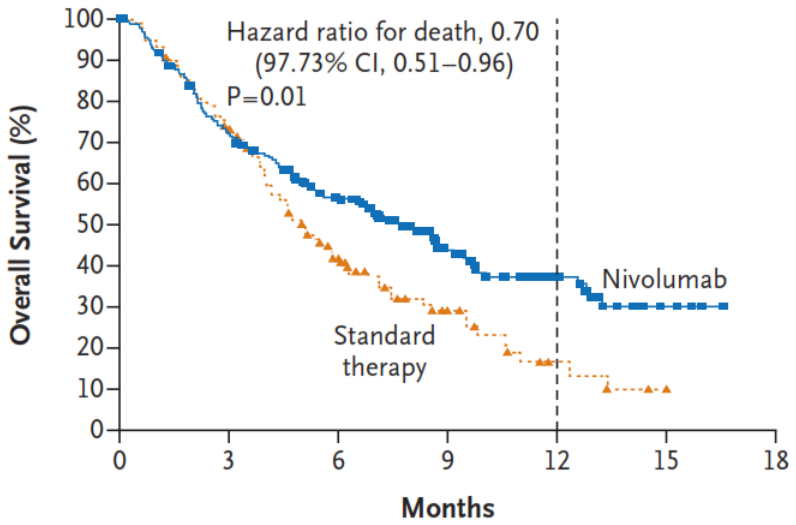
Progression-free Survival

	No. of Patients	No. of Events	Median Progression-free Survival (95% CI)
			mo
Nivolumab	240	190	2.0 (1.9–2.1)
Standard Therapy	121	103	2.3 (1.9–3.1)



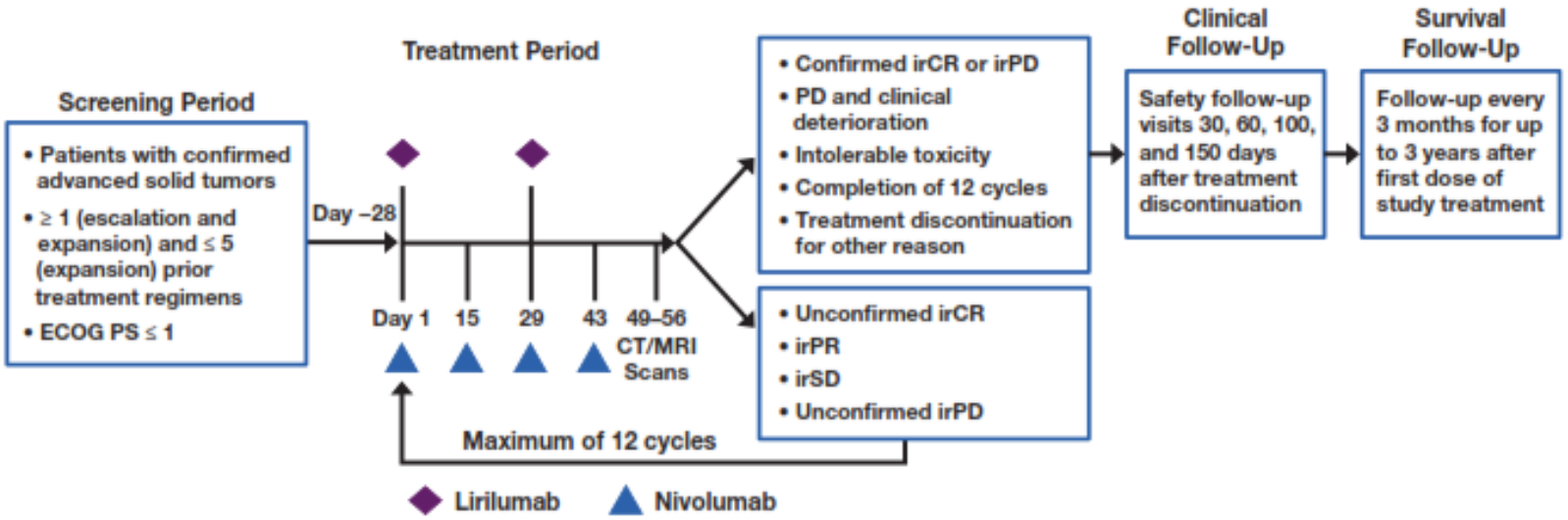
Overall Survival

	No. of Patients	No. of Deaths	1–Yr Overall Survival Rate	Median Overall Survival
			% (95% CI)	*mo (95% CI)*
Nivolumab	240	133	36.0 (28.5–43.4)	7.5 (5.5–9.1)
Standard Therapy	121	85	16.6 (8.6–26.8)	5.1 (4.0–6.0)



2016 ASCO Annual Meeting; Ferris et al, NEJM 2016

TRIAL CA223-001
TREATMENT SCHEDULE



Patients received lirilumab 0.1, 0.3, 1.0, or 3.0 mg/kg every 4 weeks + nivolumab 3 mg/kg every 2 weeks

Eligibility criteria specific to the SCCHN cohort:

> Progression or recurrence within 6 months of platinum treatment (primary or LRM setting)

> Mandatory pre- and on- treatment biopsy in 15 patients

PHASE I TRIAL OF IPH4102: BASELINE CHARACTERISTICS

Characteristics	
Median age (min/max)	71 (50-90)
CTCL subtype • MF • SS • CD4+ T cell)	 2 13 1
Stage • I-II • IV • unknown	 2 13 1
Number of prior lines of systemic therapy • 2-3 • 4-5 • 6-7 • $\geq$ 8	 5 4 4 3

PHASE I TRIAL OF IPH4102: OVERVIEW OF ADVERSE EVENTS

- 88% of the patients experienced at least 1 AE
- Vast majority were grade 1-2; only one grade 3 and one grade 4
- Only 38% of the patients experienced a treatment related AE – none were grade 3 or 4
  - > Nausea, abdominal pain, constipation, asthenia, chills, fatigue, malaise, pain, arthralgia, back pain, muscle spasm, cough, dyspnea, infusion reaction
- No DLT
- No treatment discontinuation due to an AE
- Only 4 serious AE overall and only one considered treatment related
  - > elderly patient with a history of cardiac arrhythmia developed an episode of atrial flutter; was managed with amiodarone; no recurrence upon rechallenge
- Only one death (sepsis), considered not related to treatment

PHASE I TRIAL OF IPH4102: ENCOURAGING SIGNS OF CLINICAL ACTIVITY

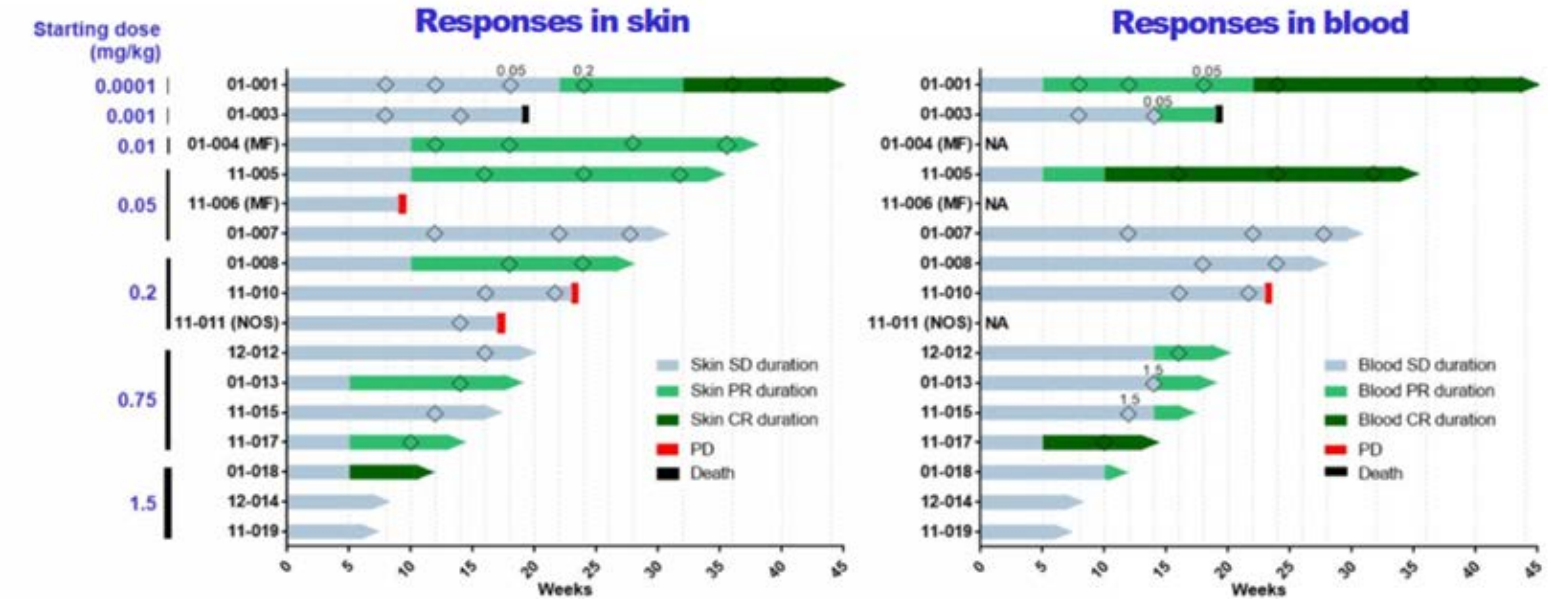
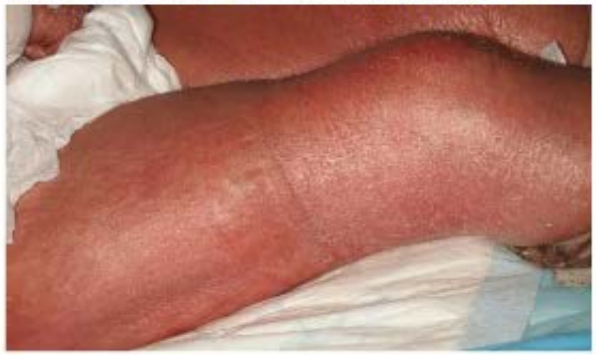
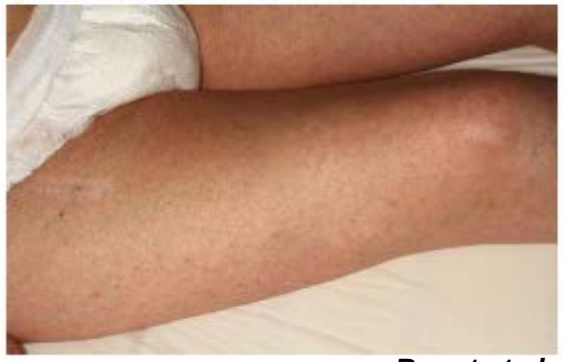


Illustration of a complete response in the skin in a 80 years old female with SS patient treated with IPH4102

06JAN2016
(W8, 0.0001 mg/kg – mSWAT (W10) = 55/2/0)



20JUL2016
(W36, 0.2 mg/kg – mSWAT = 0/0/0)



Bagot et al., 3WCCL poster 2016

PIONEER IN NK CELL MODULATION

DEVELOPING A BROAD AND DIVERSIFIED ANTIBODY PORTFOLIO

PROGRAM	TARGET	INDICATION	STAGE
Lirilumab Licensed to Bristol-Myers Squibb	KIR2DL1,2,3	Acute Myeloid Leukemia - Single agent Solid and hematological tumors - Multiple combinations	Phase II Exploratory Phase I/II program
Monalizumab Co-development with AstraZeneca	NKG2A	Solid and hematological tumors - Single agent and multiple combinations	Exploratory Phase I/II program
IPH4102	KIR3DL2	Cutaneous T-cell lymphomas	Phase I incl. cohort expansion
IPH4301	MICA/B	Cancer	IND-enabling studies
IPH52	CD39	Cancer	Research
Discovery	CD73	Cancer	Research
IPH33	TLR3	Inflammation	Research

TECHNOLOGY

NK bispecific engagers	Collaboration with Sanofi; up to two bispecific antibodies on two undisclosed tumor targets
Antibody Drug Conjugate (ADC)	