NOXXON PHARMA

Latest data from Phase 1/2 Study of NOX-A12 and pembrolizumab in patients with micro-satellite stable metastatic colorectal or pancreatic cancer

ESMO 2019 Conference Poster

30 September 2019

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Presenters

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CEO

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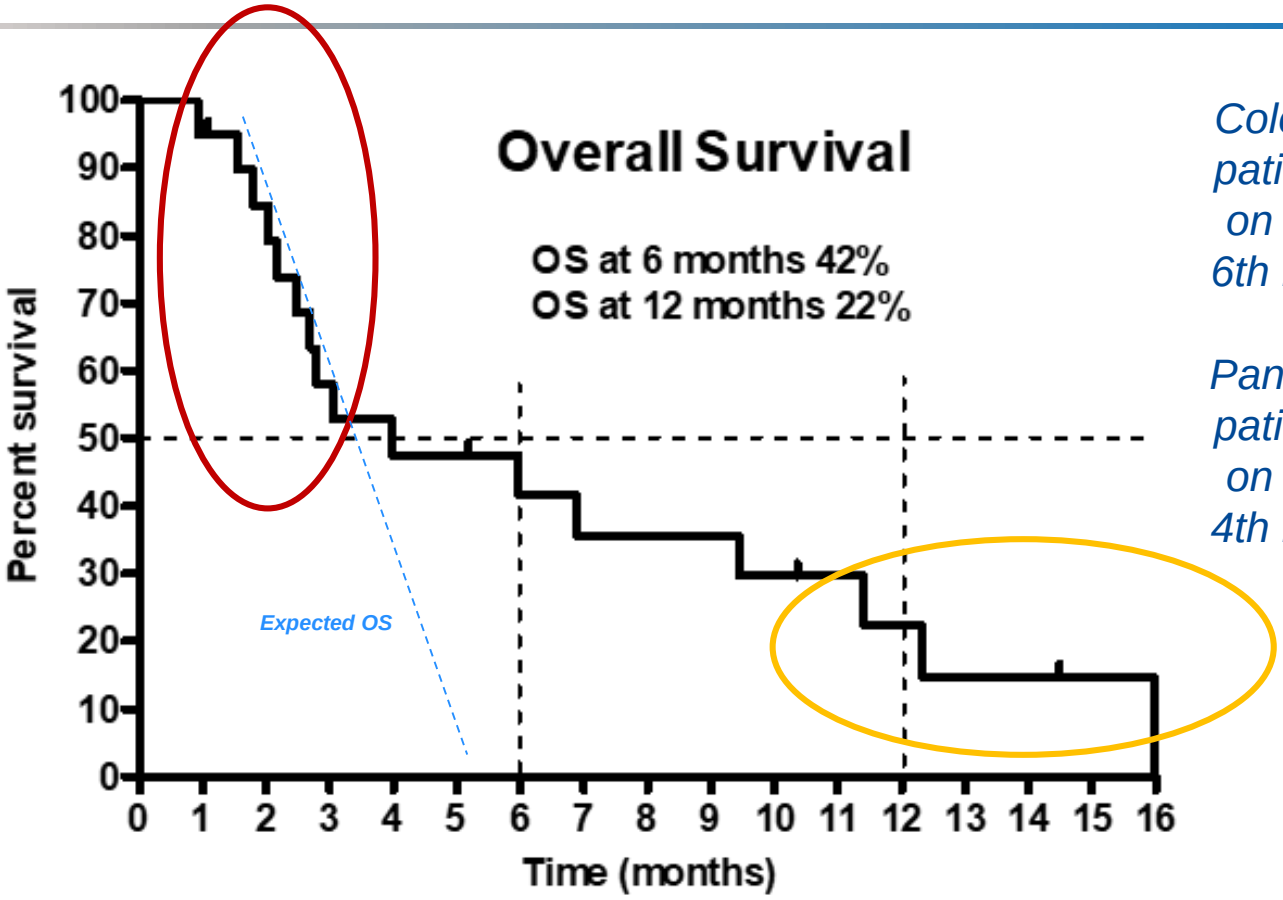
CMO

Agenda

- **Key take-aways from the Phase 1/2 NOX-A12 + immunotherapy (Keytruda®/pembrolizumab)**
  - Clinical (Overall Survival)
  - Mechanism of action
- **Where does NOX-A12 + immunotherapy fit in the NOXXON pipeline**
- **Standard of care for advanced colorectal and pancreas cancer patients**
- **Trial design, patients, outcomes in more detail**
- **Q&A**

Overall Survival Longer than expected for this Heavily Pre-Treated Population

Responses to immunotherapy can take 3-6 months to observe and many advanced patients don't have that time



month	3	6	9	12	15
# at risk	11	7	6	3	1

Colorectal cancer patients receiving on average their 6th line of therapy

Pancreatic cancer patients receiving on average their 4th line of therapy

Source: Halama et al, Phase 1/2 Study with CXCL12 Inhibitor NOX-A12 and Pembrolizumab in Patients with Microsatellite-Stable, Metastatic Colorectal or Pancreatic Cancer. ESMO Congress 2019 Poster 613P

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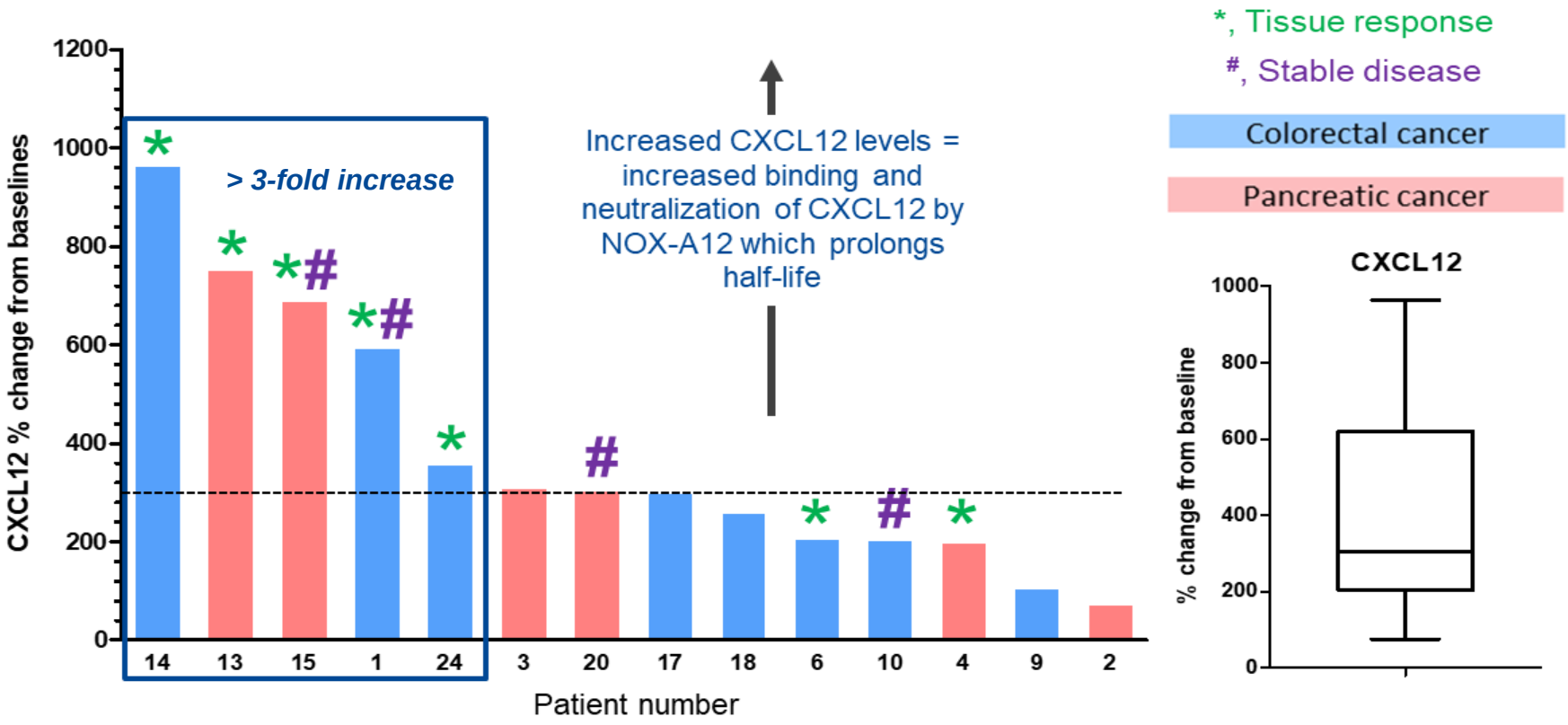
NOX-A12 Mechanism of Action Highlights – Target Neutralization, Immune Response and Stable Disease



Source: Halama et al, Phase 1/2 Study with CXCL12 Inhibitor NOX-A12 and Pembrolizumab in Patients with Microsatellite-Stable, Metastatic Colorectal or Pancreatic Cancer. ESMO Congress 2019 Poster 613P

Pipeline Assets Leverage Existing Anti-Cancer Therapies to Optimize their Therapeutic Efficacy

NOX-A12

	Indication	Combination	Preclinical / Phase 1 / Phase 2 / Phase 3
MSD	**Solid tumors** Pancreatic / Colorectal	Immunotherapy	**Phase 1/2 trial completed** Patient in follow-up ongoing Update published at Sept 2019 ESMO
Orphan Status US & EU	**Solid tumors** Brain cancer / Glioblastoma	Ablation / radiation	**Phase 1/2 trial ongoing** Clinical study initiated Sep 2019
Top-10 Pharma	**Undiclosed** Market >€1b		Preclinical evaluation to be completed Q2-2020

NOX-E36

Indication	Combination	Preclinical / Phase 1 / Phase 2 / Phase 3
Solid tumors Pancreatic / Liver	Immunotherapy & chemotherapy	**Phase 1/2a trials completed** in non-oncology indications

Trial to be completed by NOXXON

Trial to be completed with partner

All time-lines subject to financing

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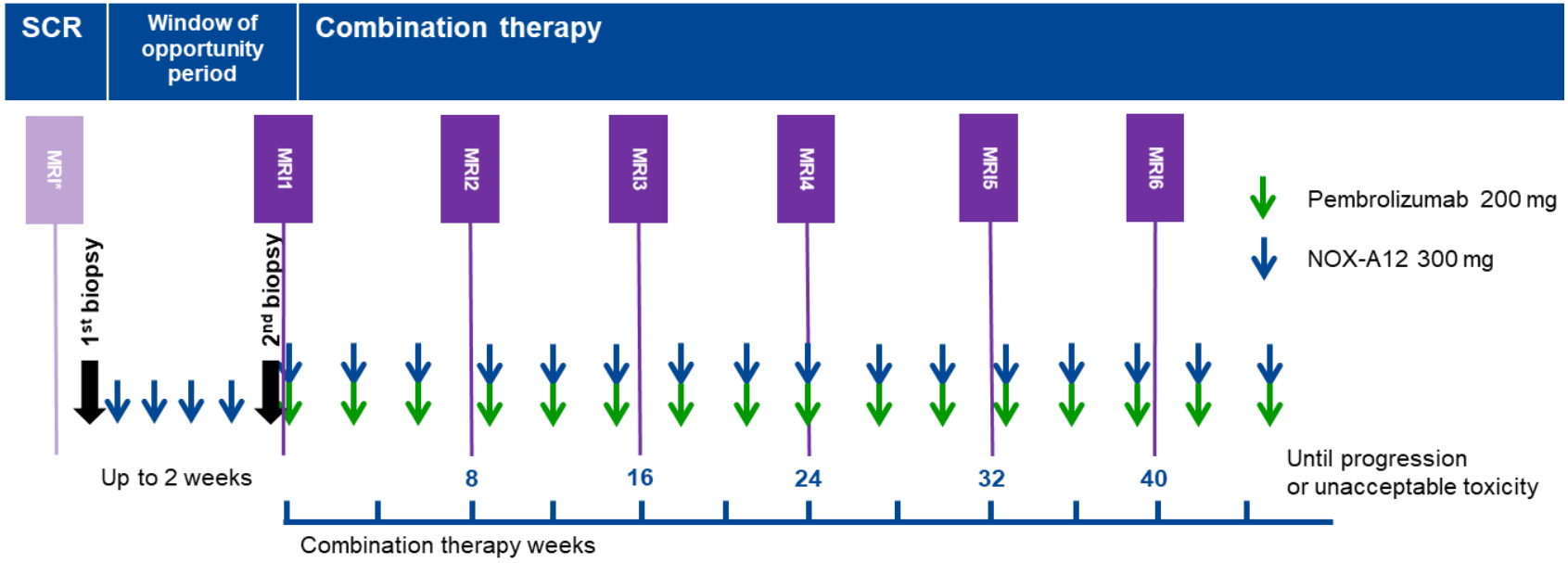
Trial Design

6th line mCRC & 4th line mPaC



Dosing

- Part A: 2 weeks of NOX-A12 monotherapy: twice per week NOX-A12
- Part B: Combination therapy: NOX-A12 + pembrolizumab given once every 3 weeks

Patient population

- All patients metastatic with liver metastases and confirmed microsatellite stable tumors
- Colorectal cancer patients receiving 6th line of therapy on average
- Pancreatic cancer patients receiving 4th line of therapy on average

Source: Halama et al, Phase 1/2 Study with CXCL12 Inhibitor NOX-A12 and Pembrolizumab in Patients with Microsatellite-Stable, Metastatic Colorectal or Pancreatic Cancer. ESMO Congress 2019 Poster 613P

Patient Demographics

	Colorectal Cancer	Pancreatic Cancer
N	11	9
Male/Female	7 / 4	8 / 1
Age, mean (range)	63 (55 – 73)	67 (48 - 82)
Stage at study entry	100% stage IV (metastatic)	
Microsatellite status at study entry	All patients MSS	
Prior lines of systemic treatment, mean (range)*	5 (2 – 9)	3 (1 – 5)
Patients with prior surgery (# of surgeries)	7 (1 – 4)	3 (1 – 2)
Best response last treatment	PD (10), SD (1)	PD (9)
Time since last systemic prior treatment (mean)	2.0 months	1.5 months

* excluding surgery

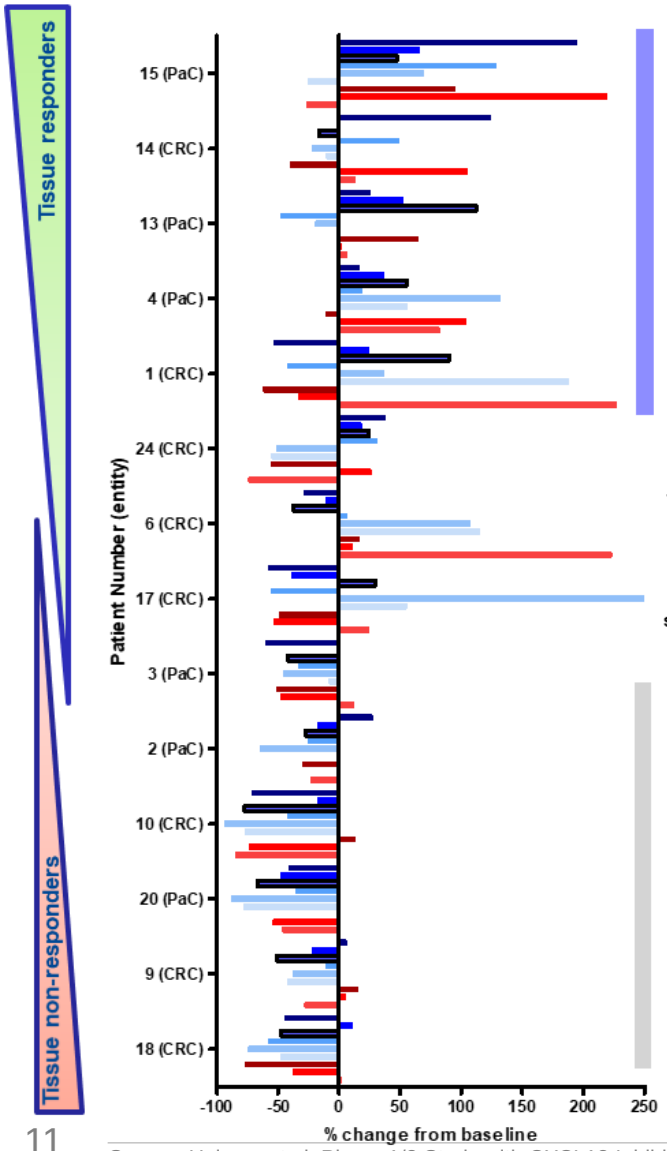
Source: Halama et al, Phase 1/2 Study with CXCL12 Inhibitor NOX-A12 and Pembrolizumab in Patients with Microsatellite-Stable, Metastatic Colorectal or Pancreatic Cancer. ESMO Congress 2019 Poster 613P

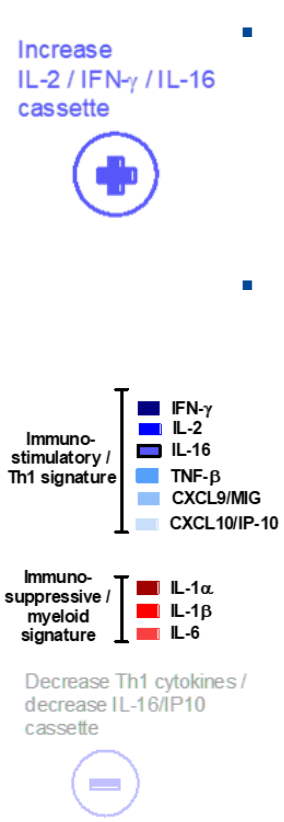
Standard of Care for Advanced Colorectal and Pancreatic Cancer Having Failed Prior Lines of Therapy

Compound Indication	Overall Respone Rate (ORR)	12- month overall survival
Lonsurf (trifluridine and tipiracil) 3rd line colorectal cancer	**1.6%** vs. 0.4%	**~27%**
Stivarga (regorafenib) 3rd line colorectal cancer	**1%** vs. 0.4%	**~25%**
Onivyde (irinotecan liposome injection) 2nd line pancreas cancer	**7.7%** vs. 0.8%	**~22%**

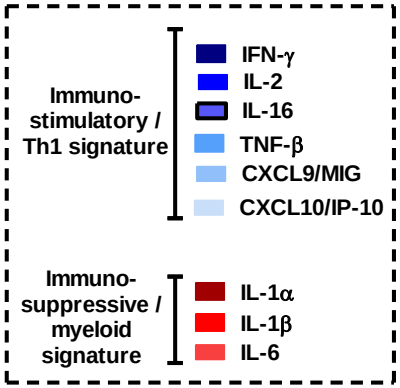
Source: respective US FDA approved product labels

NOX-A12 Monotherapy Triggers Cytokine Signatures Consistent with Th1 type Response Making the Tumor 'Hotter'





- NOX-A12 monotherapy leads to beneficial changes in the tumor microenvironment after 14 days of treatment
  - Increase in concentrations of key cytokines (IL-2 / IFN-γ / IL-16) is indicative of Th1 response
  - Th1 response, activation of cytotoxic CD8+ T cells and also of CD4+ T helper cells was found for approx. half of the patients
- Decrease in concentrations of IL-1α/β and IL-6 indicative of reduced presence or activity of myeloid-derived immunosuppressive cells



- Decrease in Th1 signature cytokines and CXCL10 indicates a decrease of T cell attraction to and activation in the tumor

Source: Halama et al, Phase 1/2 Study with CXCL12 Inhibitor NOX-A12 and Pembrolizumab in Patients with Microsatellite-Stable, Metastatic Colorectal or Pancreatic Cancer. ESMO Congress 2019 Poster 613P

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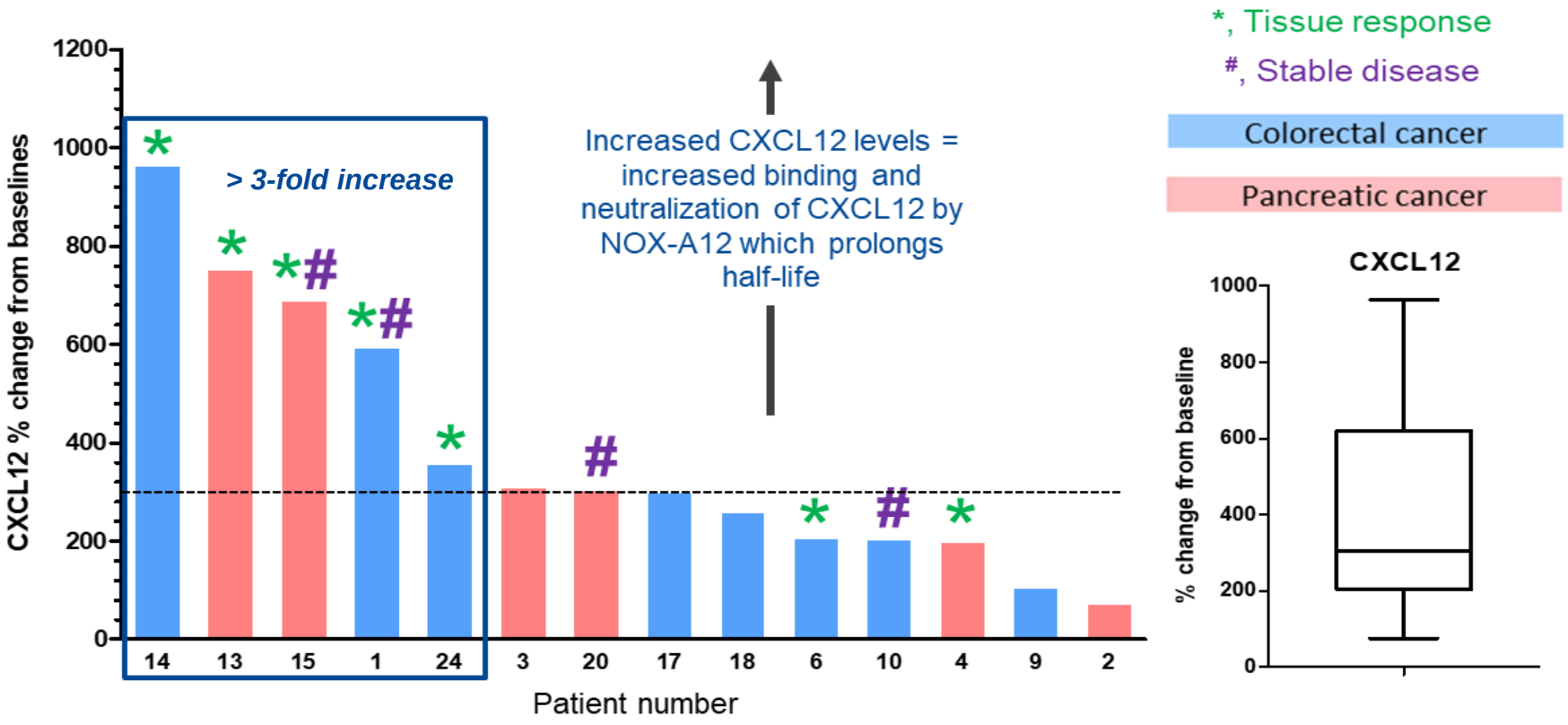
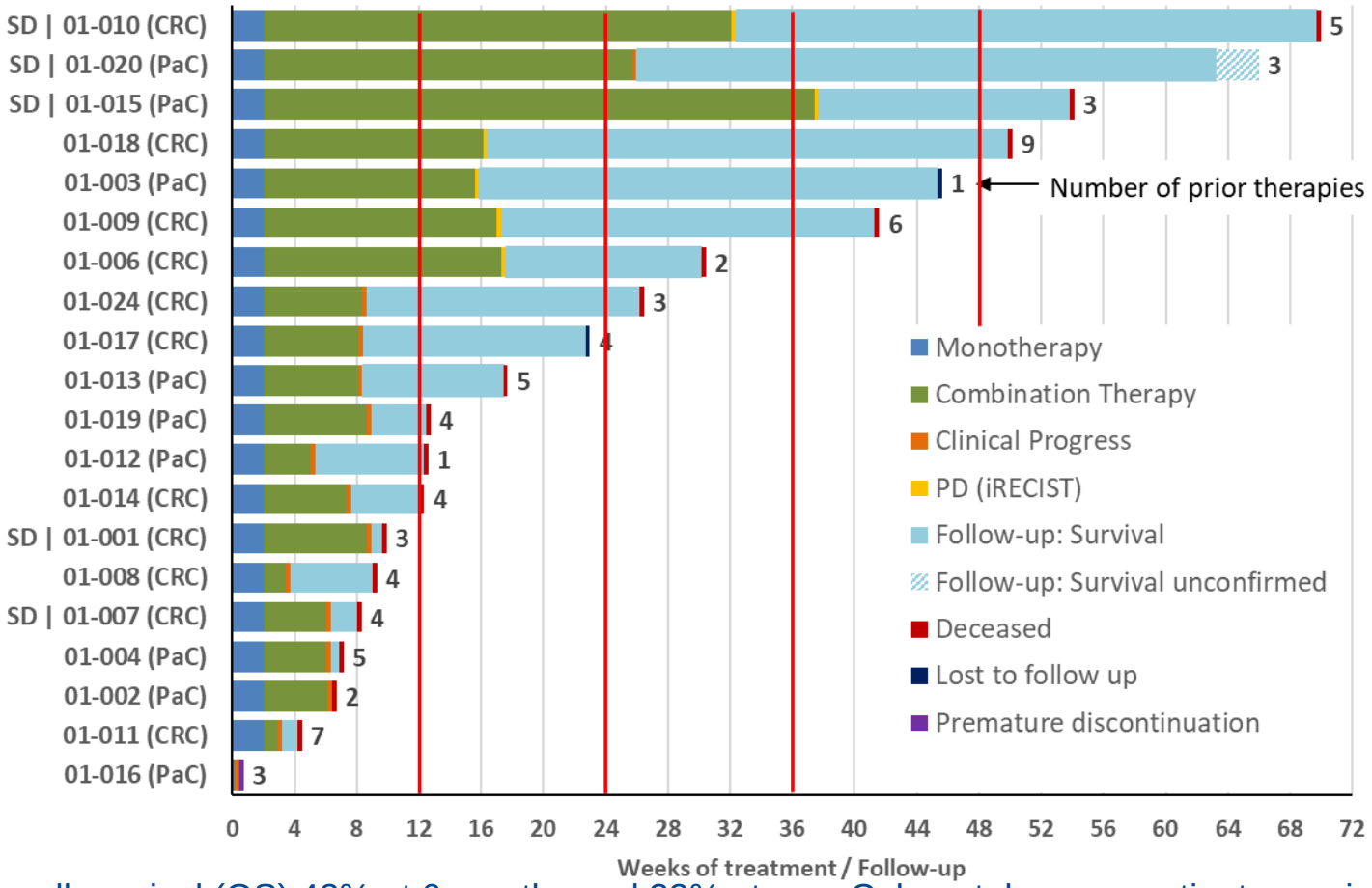
NOX-A12 Mechanism of Action Highlights – Target Neutralization, Immune Response and Stable Disease



Source: Halama et al, Phase 1/2 Study with CXCL12 Inhibitor NOX-A12 and Pembrolizumab in Patients with Microsatellite-Stable, Metastatic Colorectal or Pancreatic Cancer. ESMO Congress 2019 Poster 613P

Unexpectedly High Number of Patients with Long Time on Study



- Overall survival (OS) 42% at 6 months and 22% at 12 months
- All patients metastatic with liver metastases and confirmed microsatellite stable tumors
- Colorectal cancer patients receiving 6th line of therapy on average
- Pancreatic cancer patients receiving 4th line of therapy on average

Source: Halama et al, Phase 1/2 Study with CXCL12 Inhibitor NOX-A12 and Pembrolizumab in Patients with Microsatellite-Stable, Metastatic Colorectal or Pancreatic Cancer. ESMO Congress 2019 Poster 613P

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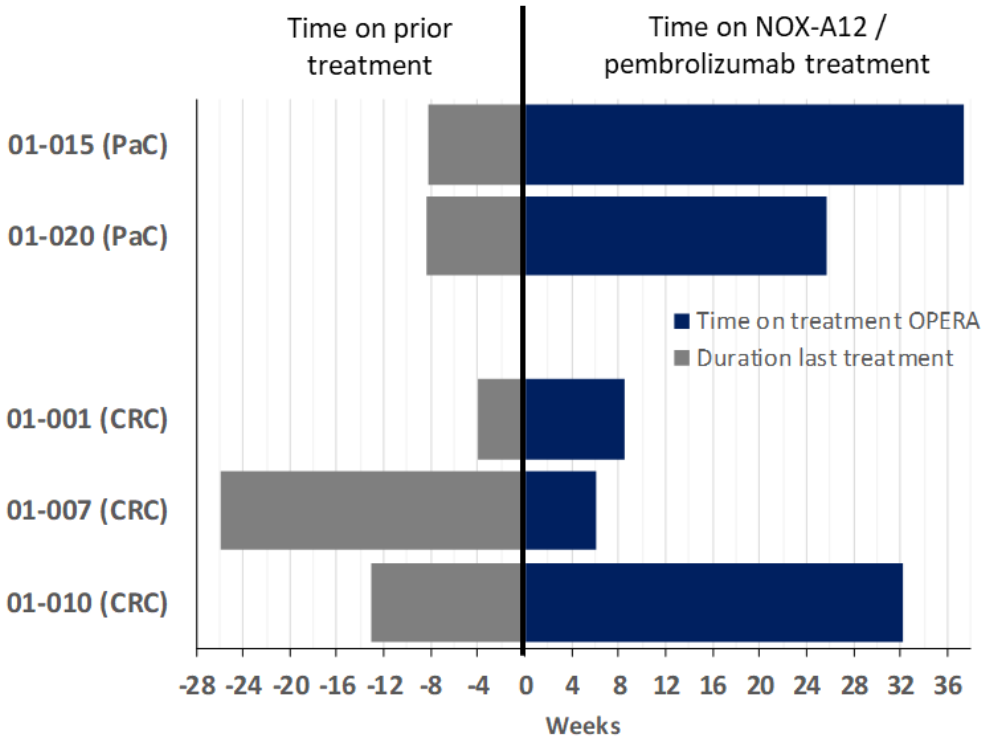
Disease Stabilization Following NOX-A12 + Keytruda® Therapy Seen in Highly Pretreated and Rapidly Progressing Patients

Duration Prior Treatment and OPERA Treatment

Patients with stable disease only



Ratio	Prior lines of treatment	Best response last treatment	Best response OPERA study
4.6	3	PD	SD
3.1	3	PD	SD
2.1	3	PD	SD
0.2	4	SD	SD
2.5	5	PD	SD

SD, Stable disease; PD, Progressive disease

Regardless of the number of prior lines of therapy or outcome of prior therapy, patients can still derive benefit extending expected progression-free survival time

Source: Halama et al, Phase 1/2 Study with CXCL12 Inhibitor NOX-A12 and Pembrolizumab in Patients with Microsatellite-Stable, Metastatic Colorectal or Pancreatic Cancer. ESMO Congress 2019 Poster 613P

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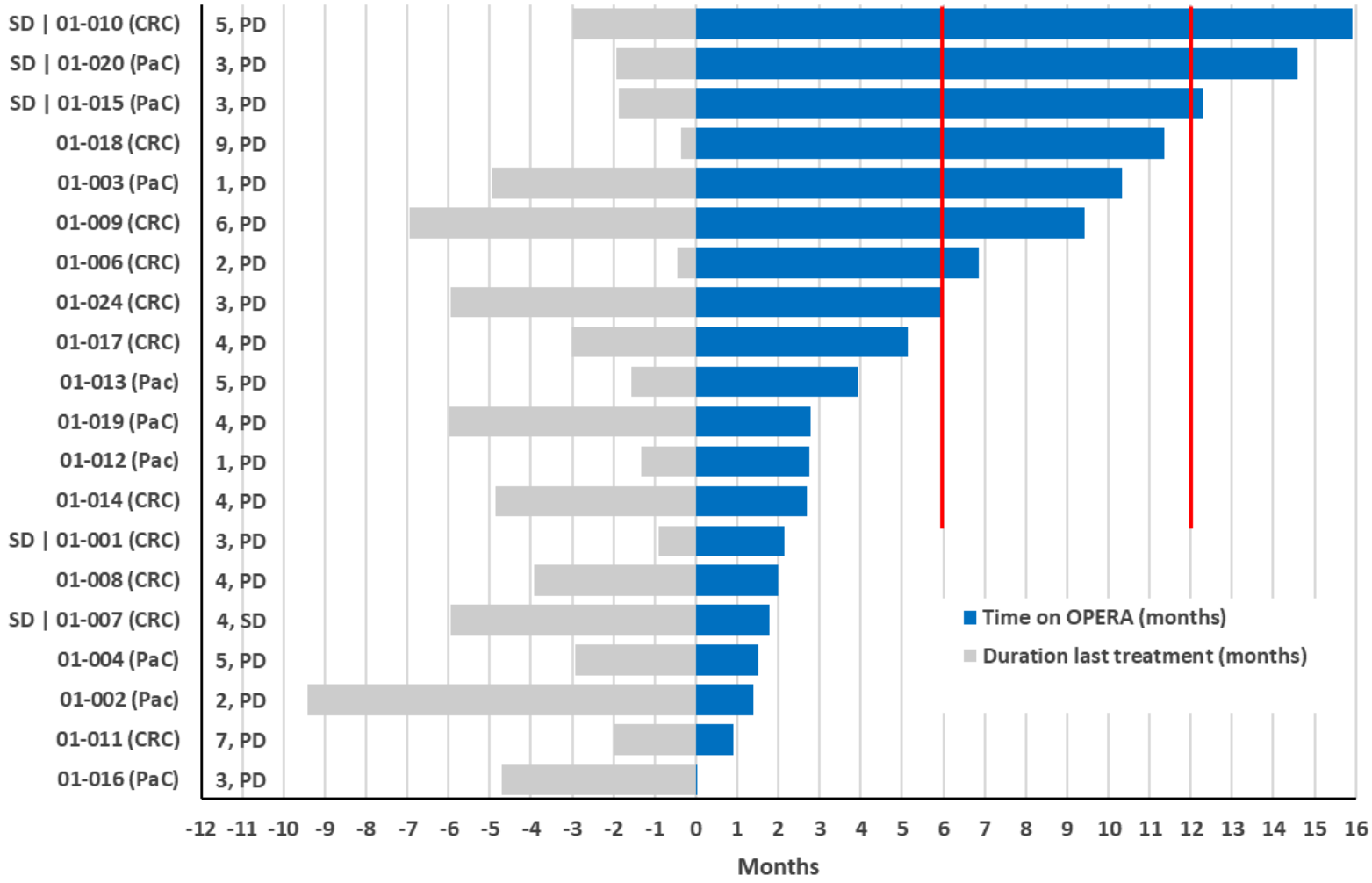
Time on Prior Therapy (Grey) vs. Time on NOX-A12 + Immunotherapy Study (Blue)



- Colorectal cancer patients receiving 6th line of therapy on average
- Pancreatic cancer patients receiving 4th line of therapy on average

Source: Halama et al, Phase 1/2 Study with CXCL12 Inhibitor NOX-A12 and Pembrolizumab in Patients with Microsatellite-Stable, Metastatic Colorectal or Pancreatic Cancer. ESMO Congress 2019 Poster 613P

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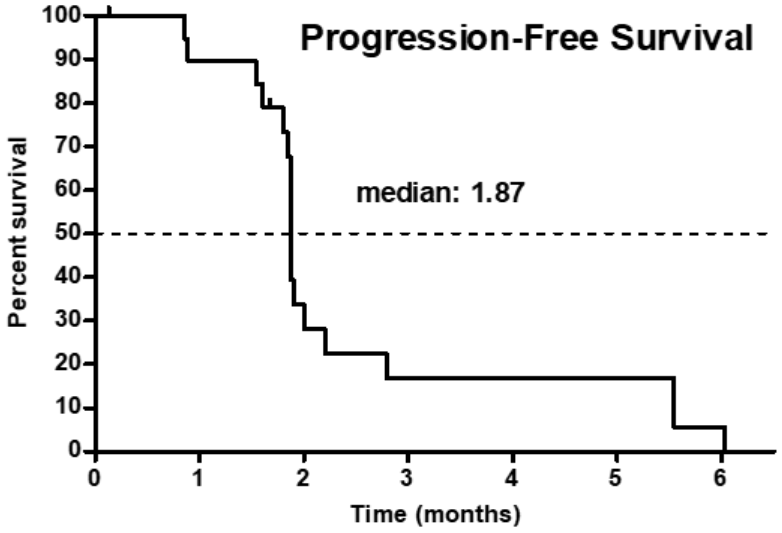
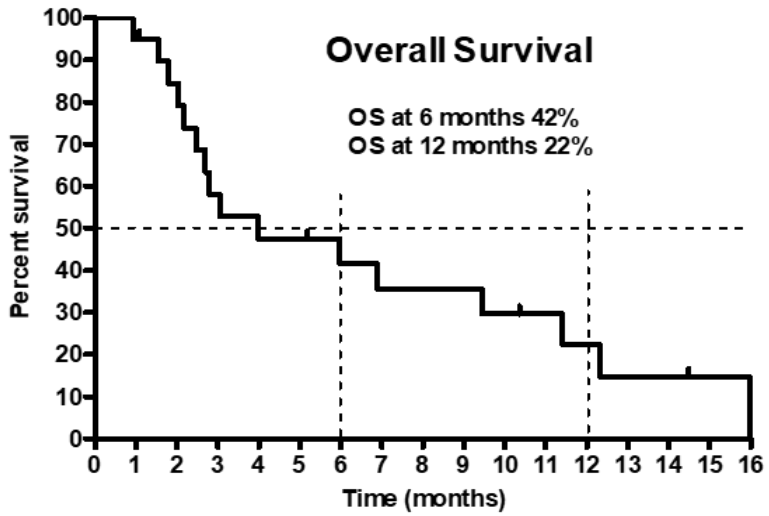
Progression-free and Overall Survival in Patients Receiving NOX-A12 + Pembrolizumab Combination Therapy



month	1	2	3	4	5	6
# at risk	17	6	3	3	3	1



month	3	6	9	12	15
# at risk	11	7	6	3	1

- Overall survival (OS) 42% at 6 months and 22% at 12 months
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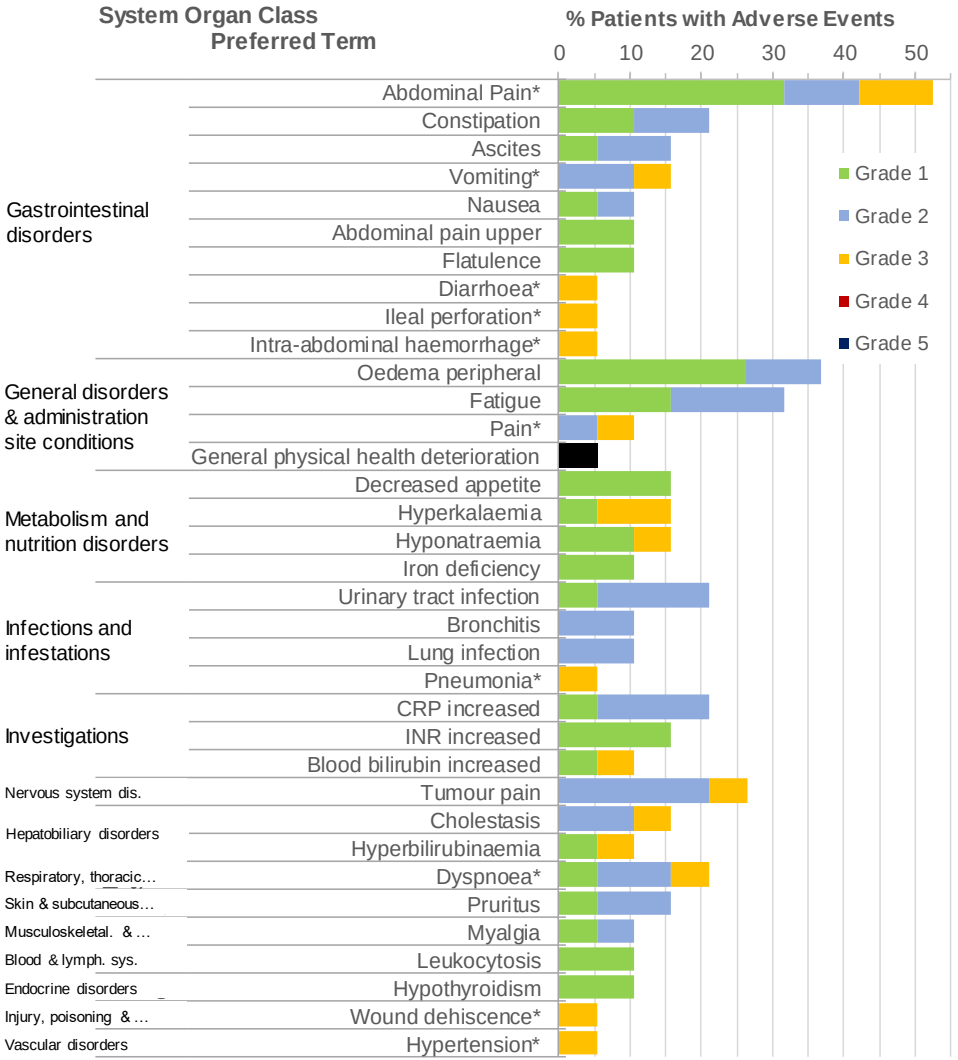
NOX-A12 Does Not Complicate Pembrolizumab Safety Profile; Ample Room to Optimize NOX-A12 Dosing

- All adverse events (AEs) are listed which were reported by at least two patients
- All reported serious adverse events (SAEs) are listed
- Six AEs are potentially related to NOX-A12; one SAE (diarrhea)
- No Grade 4 adverse events were reported
- One death / Grade 5 adverse event due to tumor progression (General physical health deterioration)
- Preferred terms including SAEs are indicated by an asterisk (*)
- Percentages are based on the total number of patients



AEs: adverse events ; SAEs: serious adverse events

Source: Halama et al, Phase 1/2 Study with CXCL12 Inhibitor NOX-A12 and Pembrolizumab in Patients with Microsatellite-Stable, Metastatic Colorectal or Pancreatic Cancer. ESMO Congress 2019 Poster 613P

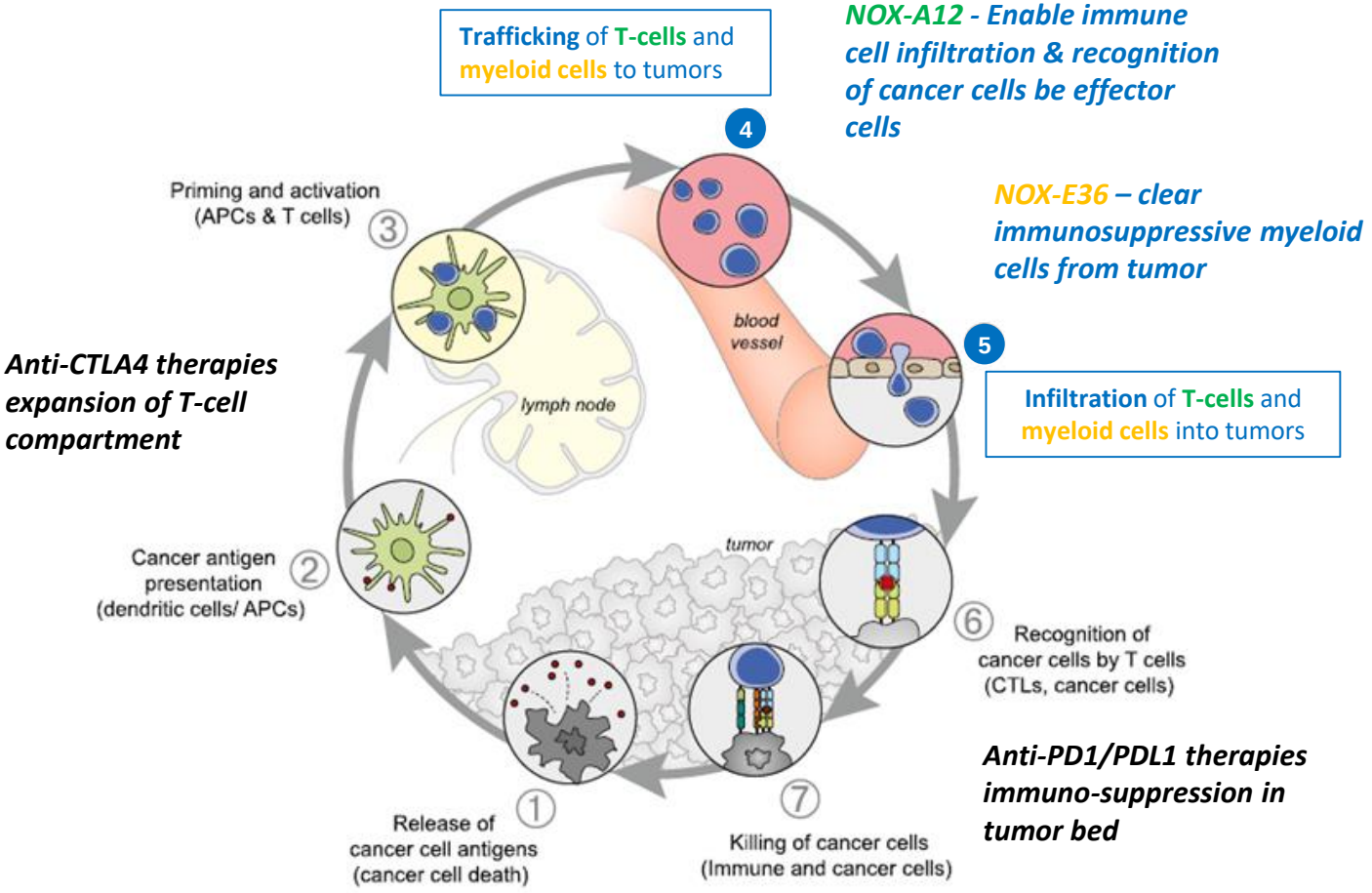
NOX-A12 Plus Keytruda® Shows Induction of Immune Response and Clinical Benefit

In MSS metastatic PaC and CRC patients with impaired immune systems and a high tumor load that have failed multiple prior lines of therapy, NOX-A12 plus Keytruda® shows induction of immune response and clinical benefit, manifesting as stable disease and prolonged time on treatment vs. prior therapy

Further studies are warranted with optimized NOX-A12 dosing and potentially additional targeting of myeloid-derived immunosuppressive cells with NOX-E36

Abbreviations: MSS: Microsatellite Stable; PaC: Pancreatic cancer ; CRC: Colorectal cancer ; AE: adverse events
Source: Halama et al 2019 ESMO Poster 613P, 2018 ESMO IO Poster 463 Presentation 84P & accompanying NOXXON Pharma Press Releases 14 Dec 2018 and 29 September 2019

Thinking about future trials – what potential combination strategies?



NOX-A12 and NOX-E36 act on key steps of the Cancer Immunity Cycle

Adapted from Chen & Mellman 2013 Immunity.

Questions ?

Thank you.

For more information do not hesitate to contact us at

Webcast@noxxon.com