da VINci: Safety and efficacy of the OTSGC-A24 vaccine and nivolumab in metastatic gastric cancer

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Background

- In metastatic gastric cancer (GC), the efficacy of single agent immunotherapy in later lines of treatment is modest.
  - KEYNOTE-061: In all comers - ORR 11%, median OS 6.7m, median PFS 1.5m[1]
  - ATTRACTION-2: ORR 11%, median OS 5.2m, median PFS 1.6m[2]

- **Cancer vaccines** involve **exogenous** administration of selected **tumor antigens** designed to activate and induce **tumor-specific cytotoxic T cells.**

- Our centre previously conducted the phase I/Ib of the OTSGC-A24 in GC demonstrating that the peptide vaccine cocktail was safe. However, single agent efficacy was modest: ORR was 0%. Stable disease (SD) 40%. Median PFS 1.7 months. Median OS 5.7 months[3].

- We hypothesize that the **combination** of **OTSGC-A24 and PD-1 blockade** will improve response rates while maintaining low toxicities.
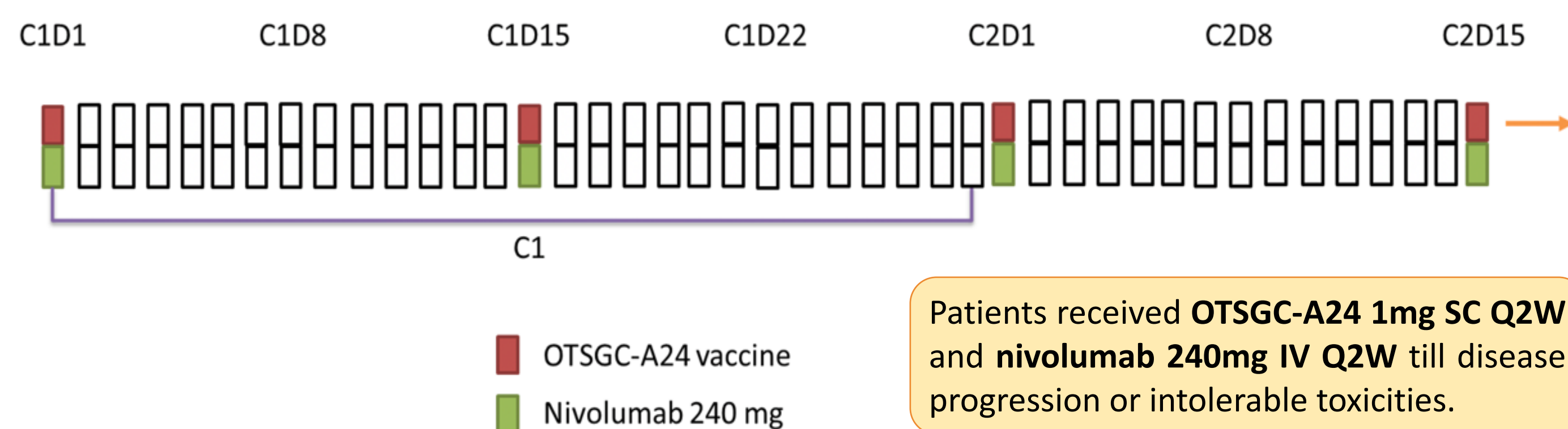
OTSGC-A24 Vaccine Components

HLA-A*24:02-binding peptides	Candidate specific antigens	Highly expressed in GC (IHC/cDNA array)
OTSGC-A24-Fo	FOXM1	60% / 61%
OTSGC-A24-De	DEPDC1	79% / 100%
OTSGC-A24-Ki	KIF20A	85% / -
OTSGC-A24-Ur-d	URLC10	76% / 100%
OTSGC-A24-VE1	VEGFR1	76%/-
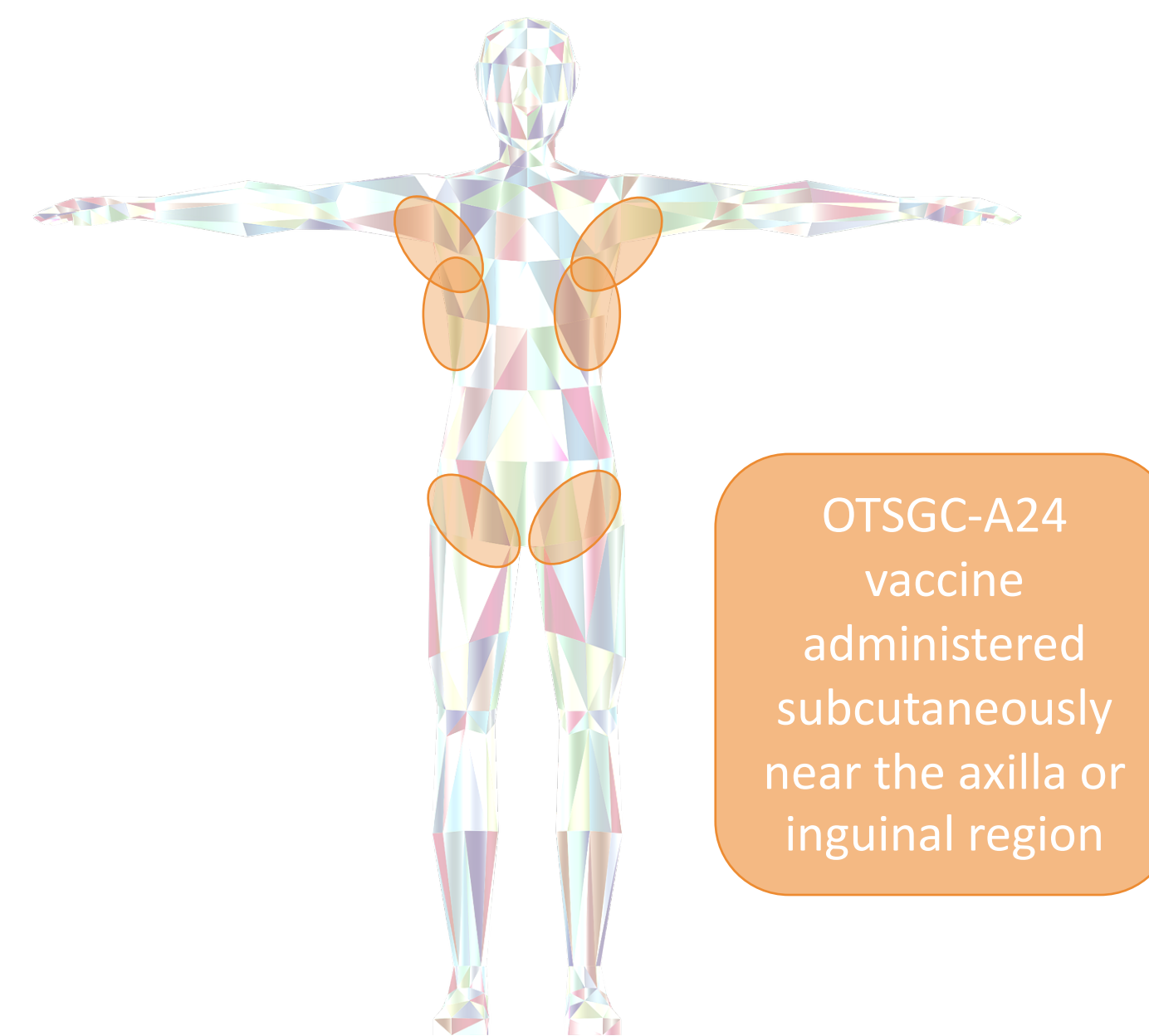
OTSGC-A24 vaccine administered subcutaneously near the axilla or inguinal region

Study Design

C1D1 C1D8 C1D15 C1D22 C2D1 C2D8 C2D15

C1

- OTSGC-A24 vaccine
- Nivolumab 240 mg

Patients received **OTSGC-A24 1mg SC Q2W** and **nivolumab 240mg IV Q2W** till disease progression or intolerable toxicities.

Primary objective: Evaluate safety of the combination of OTSGC-A24 and nivolumab.
Secondary objectives: Response rate (RECIST v1.1) and survival outcomes.

- 2 sites: National University Cancer Institute Singapore and Yonsei Cancer Centre, Seoul, Korea
- 68 patients pre-screened; 25 (**36.8%**) eligible for enrollment (HLA A*24:02 positive).
- Enrolled 18 **HLA A*24:02** subtype patients with unresectable / advanced GC
- ≥1 line of chemotherapy.
- **Immunotherapy naïve**.

Patient Characteristics

Table 1: Patient demographics and baseline characteristics

	(n=18)
Age, year (range)	Median 62.5 (46-76)
Sex, n (%)	
• Male	11 (61)
• Female	7 (39)
PS, n (%)	
• 0	6 (33)
• 1	12 (67)
Number of lines of prior chemo, n (%)	
• 1	9 (50)
• 2	4 (22)
• ≥3	5 (28)
MMR status, n (%)	
• Proficient	17 (94)
• Deficient	1 (6)

Safety

No dose limiting toxicities were observed.

Table 2: Treatment related adverse events

Adverse Events; n (%)	All Grade (n=18)	Grade 3-4 (n=18)
Infection	1 (6)	1 (6)
Fever	3 (17)	0
Gastrointestinal		
• Nausea/vomiting	3 (17)	1 (6)
• Diarrhoea	2 (11)	0
Haematological		
• Thrombocytopenia	1 (6)	0
• Leukocytosis	1 (6)	0
Endocrine		
• Hypothyroidism	2 (11)	0
• Hyperglycaemia	1 (6)	1 (6)
Hepatic		
• Raised transaminases	2 (11)	1 (6)
Injection site reaction	5 (28)	0
Respiratory		
• Cough	2 (11)	0
• Pneumonitis	1 (6)	0
Skin		
• Rash	5 (28)	1 (6)
• Pruritus	2 (11)	0
Fatigue	5 (28)	0
Raised creatinine	2 (11)	0

Results

Efficacy

Figure 1: Progression-free survival (PFS) and overall survival (OS) curves

Median PFS 1.64 months (95% CI 0.41 – 2.87)

6m PFS: 27.8%

Median OS 5.98 months (95% CI 0.76 – 11.20)

Number at risk 18 11 ... 3 2 1 1 1 1 0

Number at risk 18 11 8 6 4 3 1 1 1 1 0
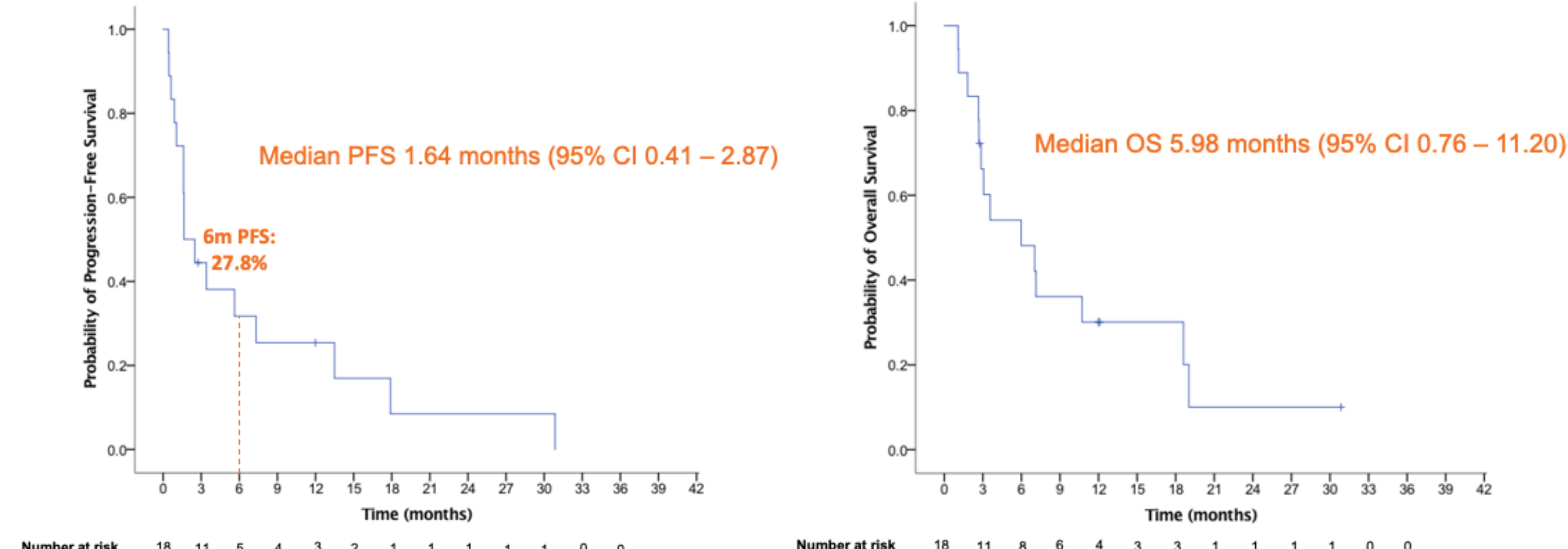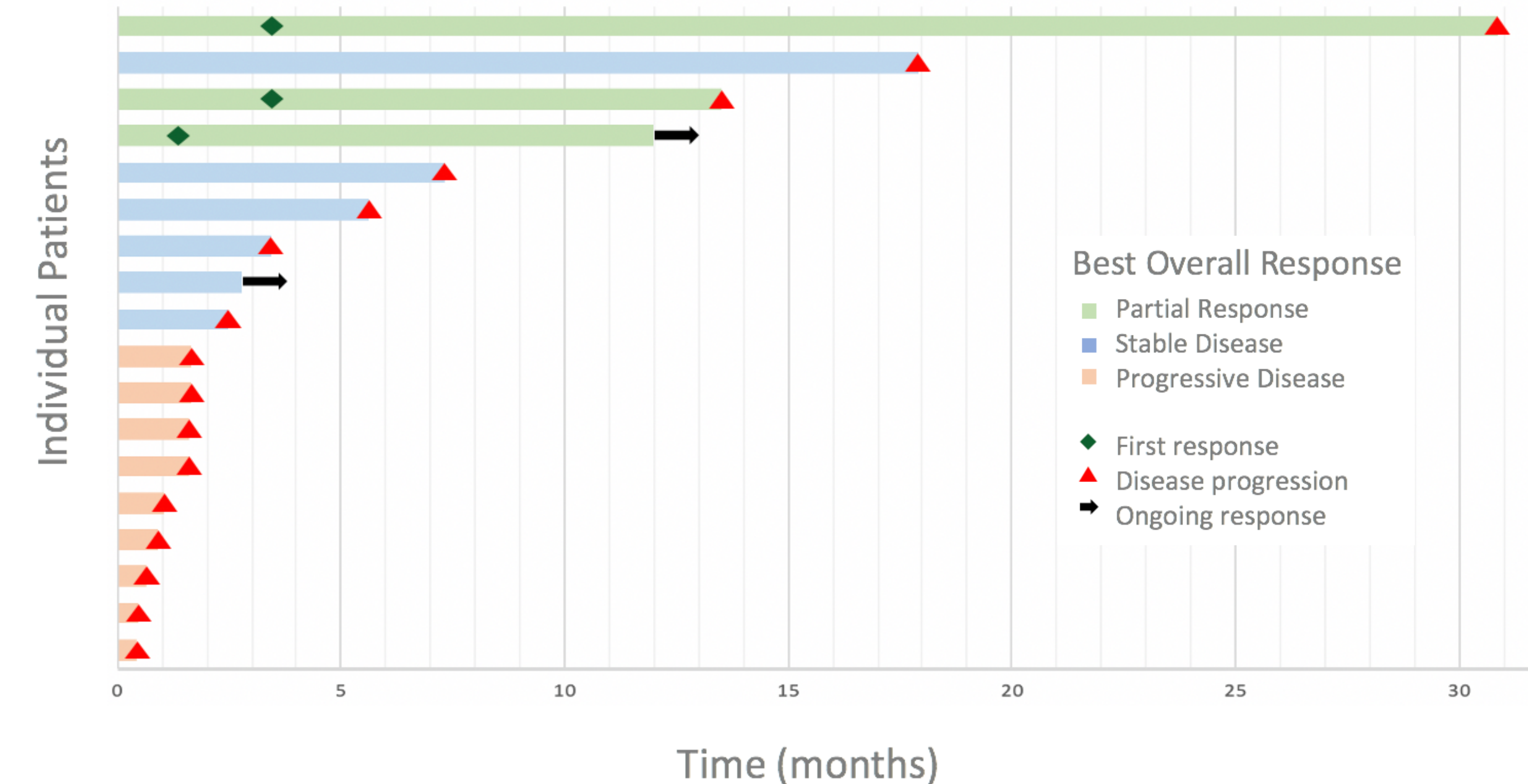
Efficacy Parameter	n=18 (%)
ORR, n (%)	
• Complete Response	0
• Partial Response	3 (16.7)
• Stable Disease	6 (33.3)
• Progressive Disease	9 (50.0)
Disease Control Rate, %	50.0
Median Duration of Response, months	13.5 months

Figure 2: Swimmers Plot

Best Overall Response
- Partial Response
- Stable Disease
- Progressive Disease

- ♦ First response
- ▲ Disease progression
- → Ongoing response

Durable clinical benefits seen in those with RECIST SD/PR. n=9 (50% of cohort)

Median PFS
13.50 months
(95% CI 4.03 - 22.98)

Median OS
18.60 months
(95% CI 3.40 - 33.79)

Conclusions

- **OTSGC-A24** in combination with **nivolumab** was **well tolerated** without any unexpected safety signals.
- The combination showed promising anti-tumor activity with **meaningful durable disease control** in metastatic GC patients previously treated with chemotherapy.
- These results support further investigation in randomized studies.
- Translational studies are underway.

References

1. Shitara et al. Lancet 2018; 392: 123–33.
2. Kang et al. Lancet 2017; 390: 2461–71.
3. Sundar et al. BMC Cancer (2018) 18:332.

Acknowledgements