

Welcome to
San Francisco!

#GI20



Welcome to
San Francisco!

#GI20

Novinky z ASCO GI 2020 - nádory jícnu a žaludku

Doc. MUDr. Igor Kiss, Ph.D.

Klinika komplexní onkologické péče MOÚ a LFMU

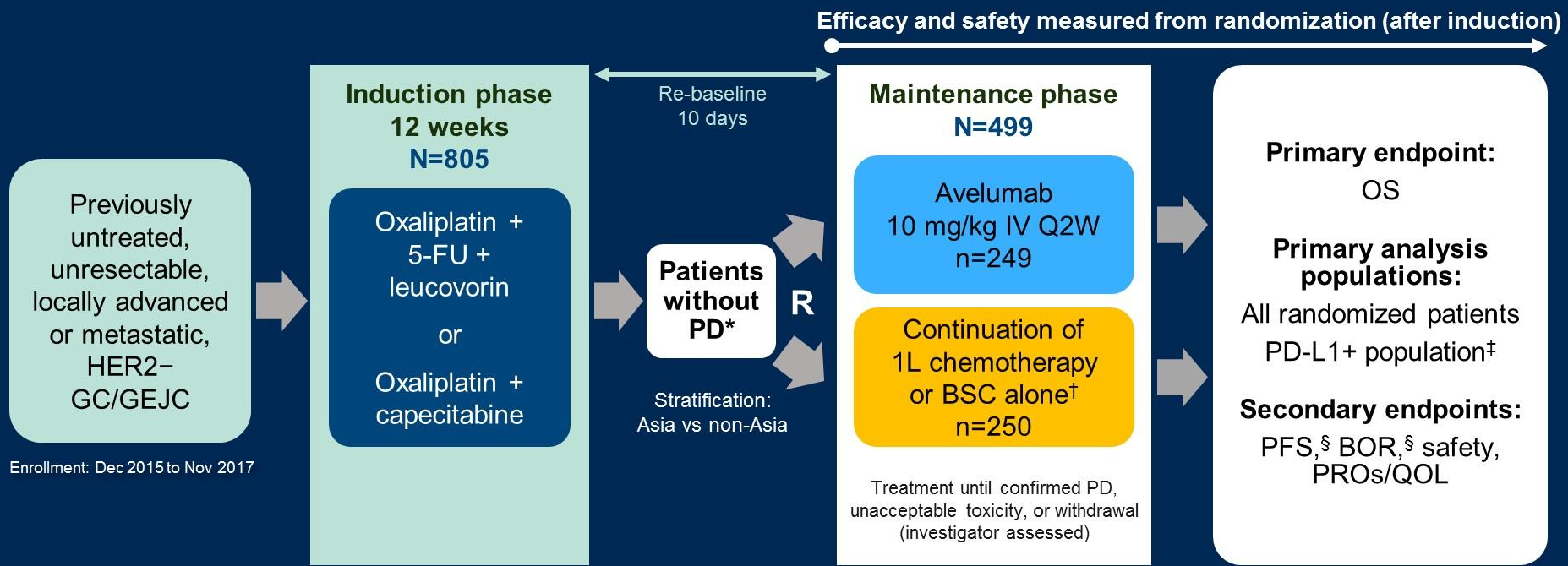
Novinky z ASCO GI 2020- nádory jícnu a žaludku

- Abstract 278: Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC). - Markus H. Moehler
- Abstract 282: Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study. - David Cunningham,
- Biomarkers to Guide Surveillance and Adjuvant Therapy of Early-Stage Disease - Yelena Yuriy Janjigian
- From Standardization to Personalized Care: How to Use Molecular Diagnostics to Guide Treatment - Harry H. Yoon

Abstract 278:

Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC). - Markus H. Moehler

JAVELIN Gastric 100: an international, open-label, phase 3 trial



1L, first-line; 5-FU, 5-fluorouracil; BOR, best overall response; BSC, best supportive care; HER2, human epidermal growth factor receptor 2; IV, intravenous; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PRO, patient-reported outcome; Q2W, every 2 weeks; QOL, quality of life; R, randomization; RECIST, Response Evaluation Criteria In Solid Tumors.
 * Eligibility for randomization based on absence of PD was confirmed by an independent radiologist. † Choice of chemotherapy or BSC decided by investigators prior to randomization.
 ‡ ≥1% of tumor cells PD-L1+ using the 73-10 pharmDx assay (Dako). § Based on investigator assessment per RECIST 1.1.

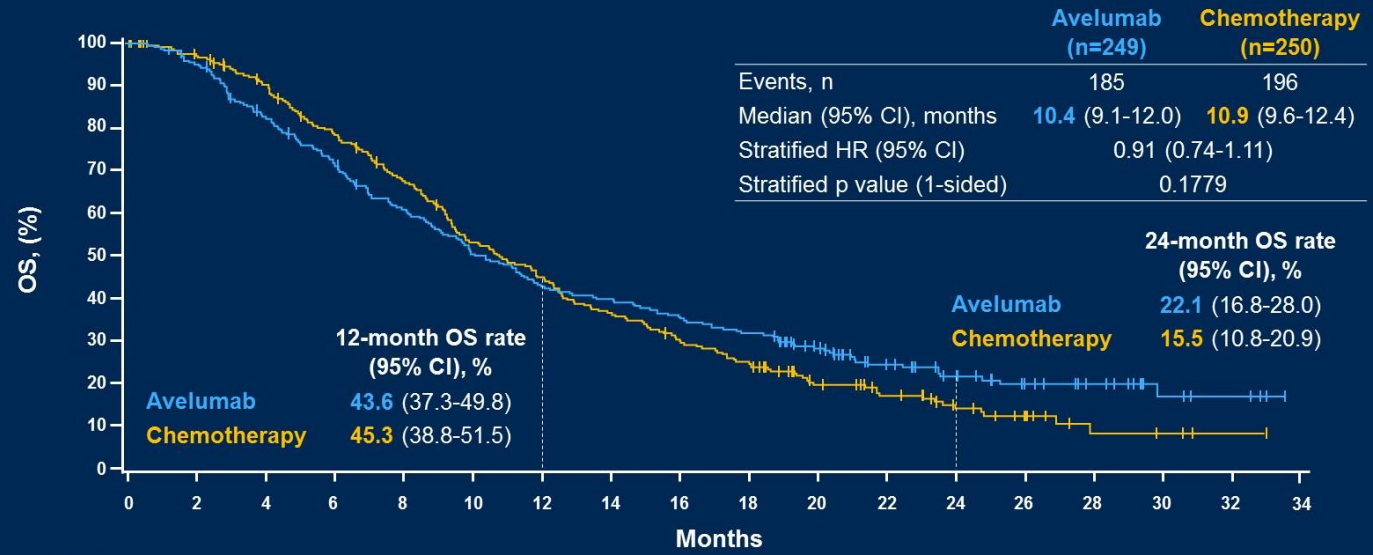
NCT02625610

Abstract 278:

Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC). - Markus H. Moehler

Primary endpoint: OS in all randomized patients (ITT)

OS was measured from randomization (after 12 weeks of induction chemotherapy)



At risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34
Avelumab	249	235	201	176	147	123	104	96	87	77	60	41	29	20	14	6	4	0
Chemotherapy	250	237	215	187	158	123	104	85	70	58	39	28	19	12	5	3	1	0

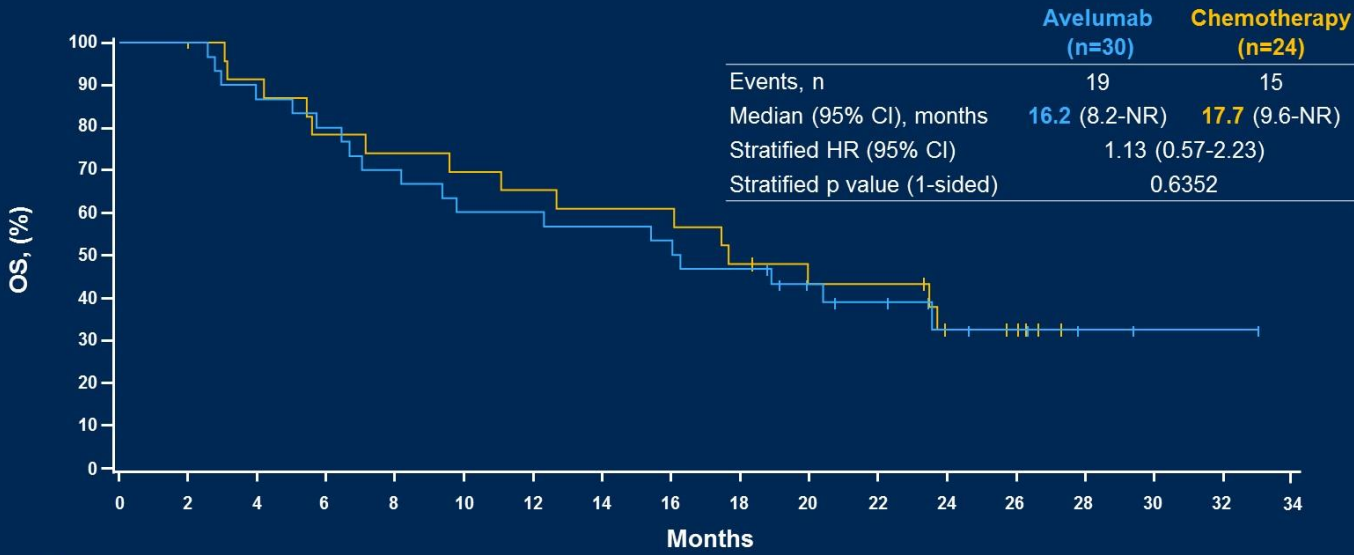
HR, hazard ratio; ITT, intention-to-treat. Minimum follow-up for OS: 18 months.

Abstract 278:

Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC). - Markus H. Moehler

Primary endpoint: OS in the PD-L1+ population (73-10 pharmDx assay; Dako)

PD-L1 cutoff: ≥1% of tumor cells (prevalence: 12.3% of evaluable patients [54/438])



At risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34
Avelumab	30	30	26	24	21	18	18	17	16	14	10	8	5	4	2	1	1	0
Chemotherapy	24	23	21	18	17	16	15	14	14	11	10	9	5	4	0	0	0	0

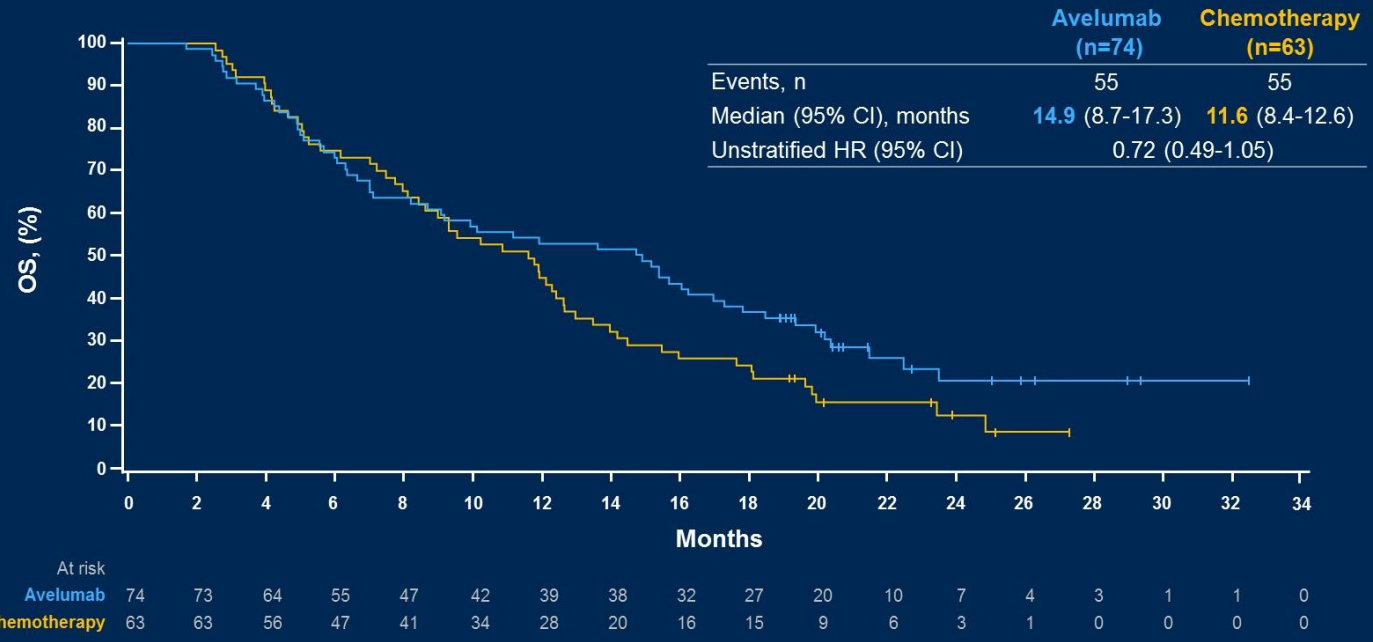
NR, not reached.
OS was measured from randomization (after 12 weeks of induction chemotherapy).

Abstract 278:

Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2- advanced gastric or gastroesophageal junction cancer (GC/GEJC). - Markus H. Moehler

Exploratory analysis: OS in the PD-L1+ population (22C3 pharmDx assay; Dako)

PD-L1 cutoff: CPS ≥1 (prevalence: 64.3% of evaluable patients [137/213])



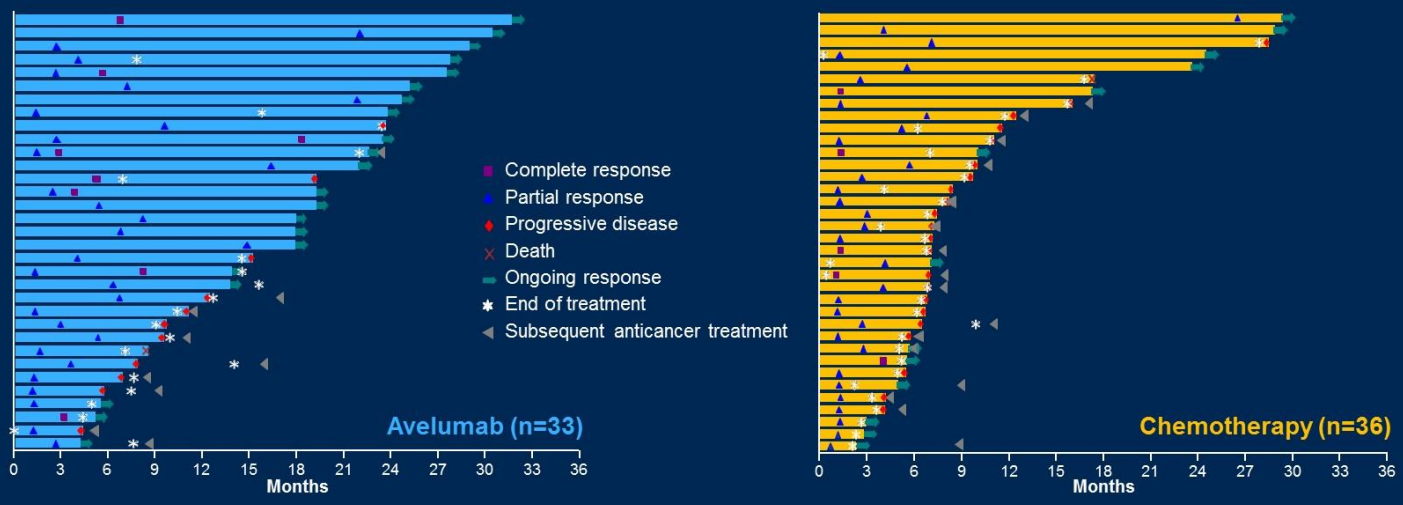
*CPS = (# of PD-L1+ cells [tumor cells, lymphocytes, or macrophages]/total # of viable cells) × 100

Abstract 278:

Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2- advanced gastric or gastroesophageal junction cancer (GC/GEJC). - Markus H. Moehler

Time to and duration of response from randomization

Responses in patients with PR or SD after induction chemotherapy (excludes 10 patients with CR during induction)



	Avelumab (n=33)	Chemotherapy (n=36)
Median duration of response	Not reached (95% CI: 9.7-NR)	5.9 months (95% CI: 4.5-7.2)
Proportion ongoing		
at 12 months:	62.3% (95% CI: 40.9-77.9)	28.4% (95% CI: 13.2-45.7)
at 24 months:	51.0% (95% CI: 29.0-69.4)	13.5% (95% CI: 3.1-31.6)

Abstract 278:

Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC). - Markus H. Moehler

Safety overview

	Avelumab (n=243)	Chemotherapy (n=238)
Any AE (related or unrelated), % (n) Grade ≥3	91.8 (223) 54.3 (132)	89.9 (214) 53.8 (128)
Any TRAE, % (n) Grade ≥3	61.3 (149) 12.8 (31)	77.3 (184) 32.8 (78)
TRAE leading to permanent discontinuation, % (n)*	10.3 (25)	27.3 (65)
Serious TRAE, % (n)	7.8 (19)	9.7 (23)
TRAE leading to death, % (n)	0	0.4 (1)
Infusion-related reaction of any grade, % (n)†	19.8 (48)	7.1 (17)

TRAE, treatment-related adverse event.

* TRAEs leading to discontinuation in ≥1% of patients were: avelumab, pneumonitis (1.6%); chemotherapy, peripheral sensory neuropathy (7.6%), peripheral neuropathy (6.7%), neutropenia (2.1%), neurotoxicity (2.1%), thrombocytopenia (1.7%), decreased appetite (1.3%).

† Identified using an expanded definition that included both a prespecified list of MedDRA preferred terms (infusion-related reaction, drug hypersensitivity, anaphylactic reaction, or hypersensitivity reaction) that occurred on the day of infusion or the following day, and prespecified signs/symptoms that occurred on the day of infusion and resolved within 2 days (related or unrelated).

PRESENTED AT:

Gastrointestinal
Cancers Symposium

Slides are the property
of the author, permission
required for reuse.

PRESENTED BY:

Markus Moehler, MD

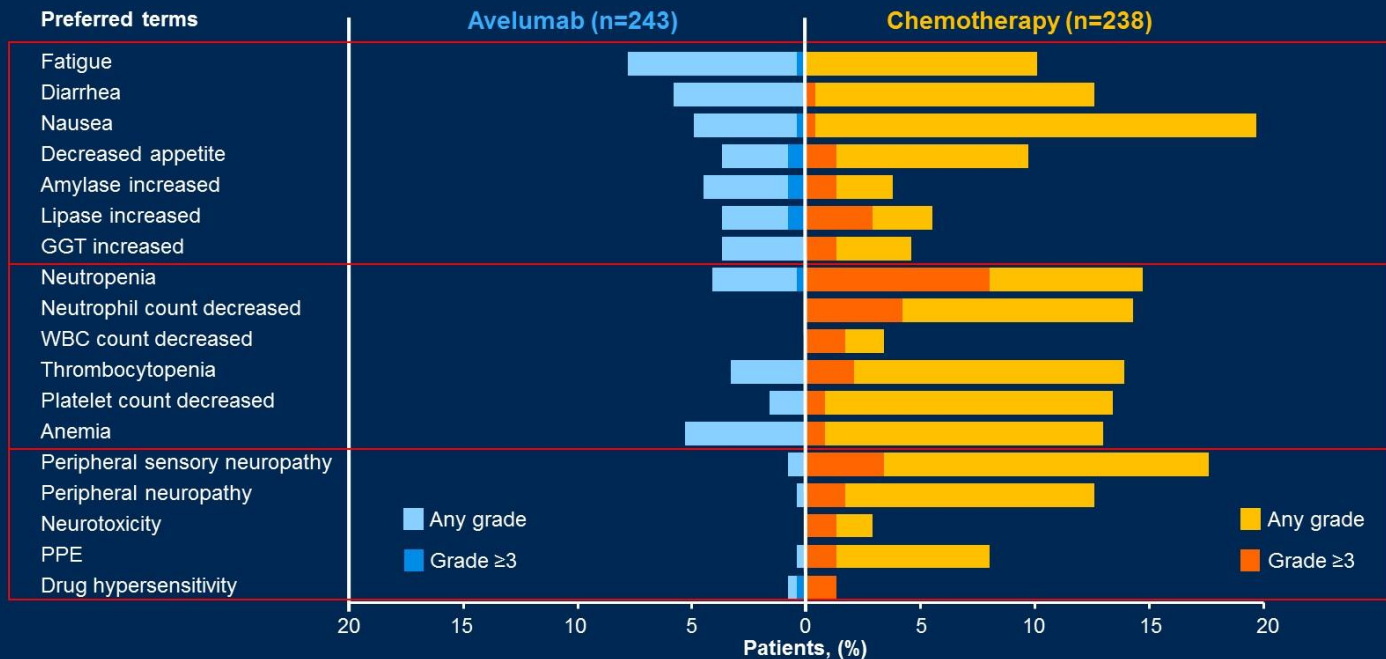
#G120

Abstract 278:

Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC). - Markus H. Moehler

Treatment-related adverse events

Any grade in $\geq 10\%$ or grade ≥ 3 in $\geq 1\%$ of either arm



GGT, gamma-glutamyltransferase; PPE, palmar-plantar erythrodysesthesia syndrome; WBC, white blood cell.

PRESENTED AT:

Gastrointestinal
Cancers Symposium

Slides are the property
of the author, permission
required for reuse.

PRESENTED BY:

Markus Moehler, MD

#G120

Abstract 278:

Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC). - Markus H. Moehler

- **Studie JAVELIN 100**

- neprokázala ve srovnání s udržovací chemoterapií zlepšený výsledek OS a to ani se zohledněním PD-L+
- udržovací léčba avelumabem prokázala však
 - delší trvání RR,
 - menší toxicitu

Novinky z ASCO GI 2020- nádory jícnu a žaludku

- Abstract 278: Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC). - Markus H. Moehler
- **Abstract 282: Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study.** - David Cunningham,
- Biomarkers to Guide Surveillance and Adjuvant Therapy of Early-Stage Disease - Yelena Yuriy Janjigian
- From Standardization to Personalized Care: How to Use Molecular Diagnostics to Guide Treatment - Harry H. Yoon

Abstract 282: Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study. - David Cunningham,

Study design

- PLATFORM is a prospective, open-label, multi-centre, randomised phase II trial assessing maintenance therapy in OGA
- Adaptive design
- 6 arms currently recruiting (HER2 negative cohort: 5 arms; HER2 positive cohort: 1 arm)
 - 154 patients/arm
 - Estimated total accrual: 924 patients
- Primary endpoint: Progression-free survival (PFS)

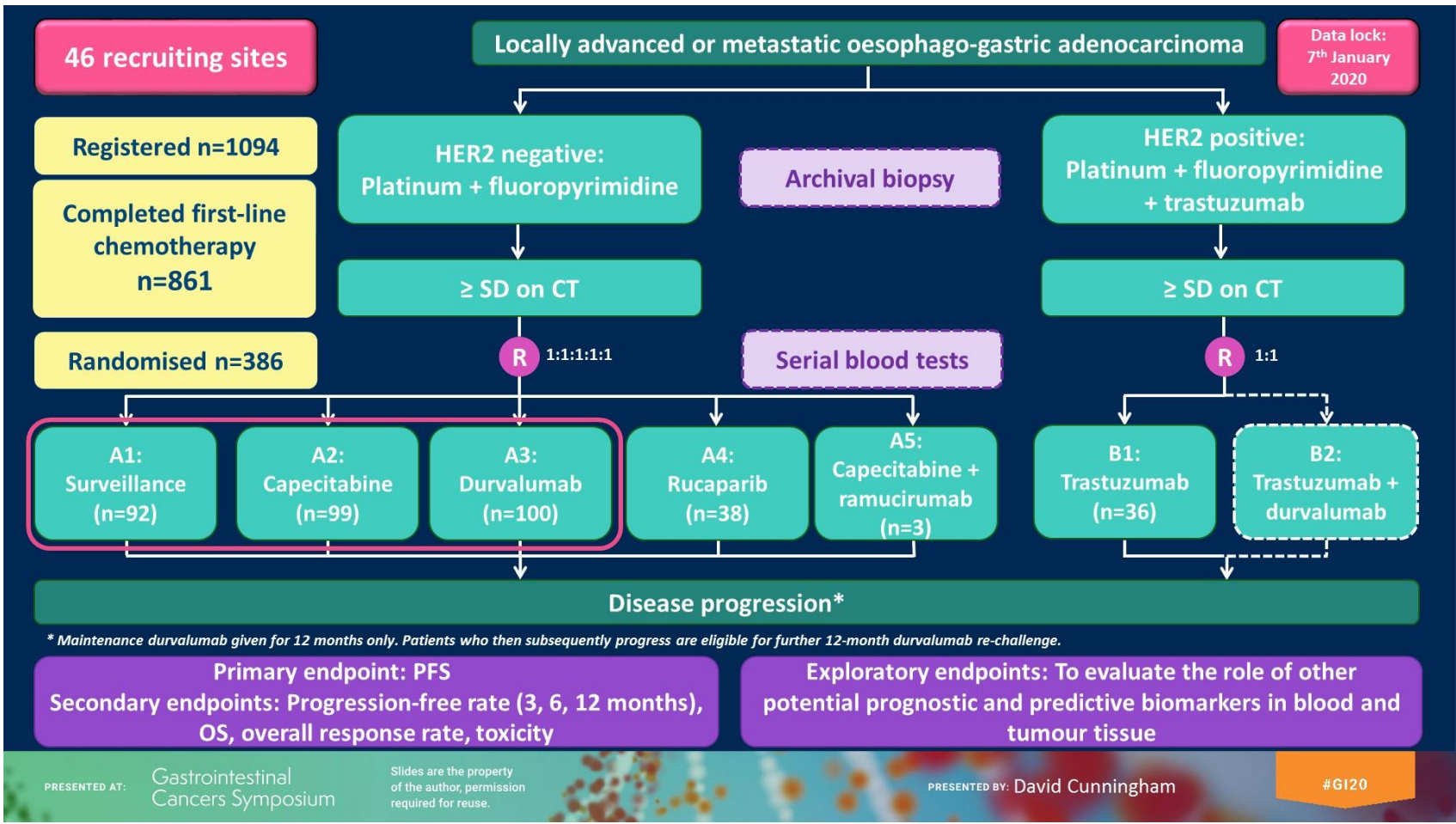
INTERIM ANALYSIS

Triggered when **61** patients/arm recruited and evaluable at 12 weeks

Endpoint: Progression-free rate (PFR) at 12 weeks

Individual arms will continue accrual if the upper limit of 1-sided 95% CI around the difference in PFR is >0 when compared to A1.

Abstract 282: Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study. - David Cunningham,



Abstract 282: Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study. - David Cunningham,

Progression-free rate (PFR) at 12 weeks from randomisation

Treatment arms	A1: Surveillance (n=61)	A2: Capecitabine (n=61)	A3: Durvalumab (n=61)
PFR at 12 weeks (95% CI)	30 (49%) (39, 60%)	34 (56%) (45, 66%)	29 (48%) (37, 58%)
PFR compared to A1 (95% CI)	Control	+6.6% (-8.3, +21.4%)	-1.6% (-16.5, +13.3%)

Treatment arms	A1: Surveillance (n=61)	A2: Capecitabine (n=61)	A3: Durvalumab (n=61)
Complete response (CR)	0 (0%)	0 (0%)	0 (0%)
Partial response (PR)	0 (0%)	0 (0%)	3 (5%)
Stable disease (SD)	30 (49%)	34 (56%)	26 (43%)
Progressive disease (PD)	28 (46%)	25 (41%)	31 (51%)
Clinical PD	3 (5%)	2 (3%)	1 (2%)

Abstract 282: Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study. - David Cunningham,

PFR at 12 weeks by PD-L1 status and tumour mutational burden (TMB)

PD-L1 quantified using Tumor and Tumor-associated Immune Cell (TIC) score

Median TMB: 5.8 mutations/Mb (range: 1.0-78.1)
 Median TMB A1: 5.3 (range: 2.1-78)
 Median TMB A3: 5.9 (range: 1.0-53)
 Low: 1.0-4.3 Medium: >4.3-8.5 High: >8.5-79

Treatment arm	A1: Surveillance (n=44)		A3: Durvalumab (n=38)	
PD-L1	TIC ≥1 n=28	TIC ≥10 n=7	TIC ≥1 n=22	TIC ≥10 n=4
Progression-free	15 (54%)	3 (43%)	14 (64%)	4 (100%)
Progressive disease	13 (46%)	4 (57%)	8 (36%)	0 (0%)

Treatment arm	A1: Surveillance (n=37)			A3: Durvalumab (n=36)		
TMB	Low n=14	Medium n=9	High n=14	Low n=11	Medium n=15	High n=10
Progression-free	9 (64%)	2 (22%)	8 (57%)	7 (64%)	6 (40%)	8 (80%)
Progressive disease	5 (36%)	7 (78%)	6 (43%)	4 (36%)	9 (60%)	2 (20%)

CD4 and CD8 infiltration according to PD-L1 and TMB

Biomarker	T cells		
	Low	Medium	High
PD-L1 TIC ≥10	3/29 (10%)	2/17 (12%)	6/28 (21%)
TMB high	13/26 (50%)	6/15 (40%)	3/24 (13%)

Abstract 282: Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study. - David Cunningham,

Grade ≥3 Treatment-related adverse events (TrAEs)

Maximum reported grade of TrAEs (Grades ≥3 only)			
Grade	A1: Surveillance (n=61)	A2: Capecitabine (n=61)	A3: Durvalumab (n=61)
3	0 (0%)	8 (13%)	7 (11%)
4	0 (0%)	0 (0%)	2 (3%)
5	0 (0%)	0 (0%)	0 (0%)

A2: Capecitabine Grade 3 TrAEs:

- Fatigue (5%), peripheral sensory neuropathy (3%), anaemia (2%), dysgeusia (2%), hand-foot syndrome (2%), hypoalbuminaemia (2%), hyponatraemia (2%), pain (2%).

A3: Durvalumab Grade 3/4 TrAEs:

- Raised ALT (5%), hyperbilirubinaemia (4%), diarrhoea (3%), raised AST (2%), raised GGT (2%), anaemia (2%), hypoalbuminaemia (2%), fatigue (2%), ascites (2%), chills (2%), hypertension (2%), hypophosphataemia (2%), pleural effusion (2%)

Abstract 282: Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study. - David Cunningham,

- Interní analýza studie PLATFORM
 - Studie pokračuje
 - Radiologická RR byla jen v rameni durvulumabem
 - Efekt byl výraznější ve skupině PD-L + a TMB

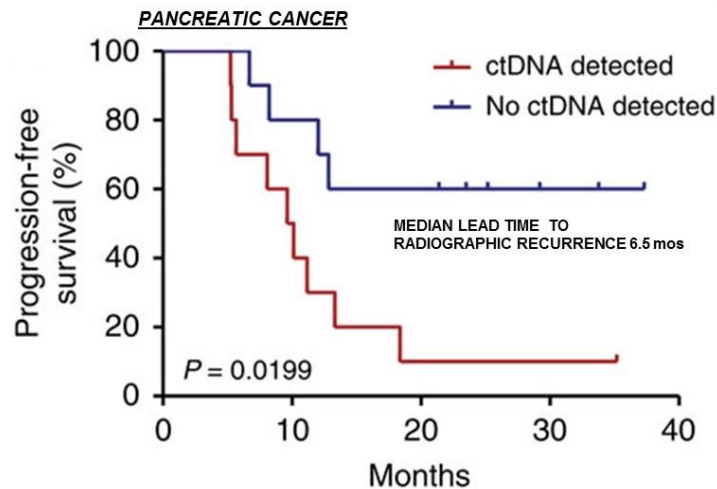
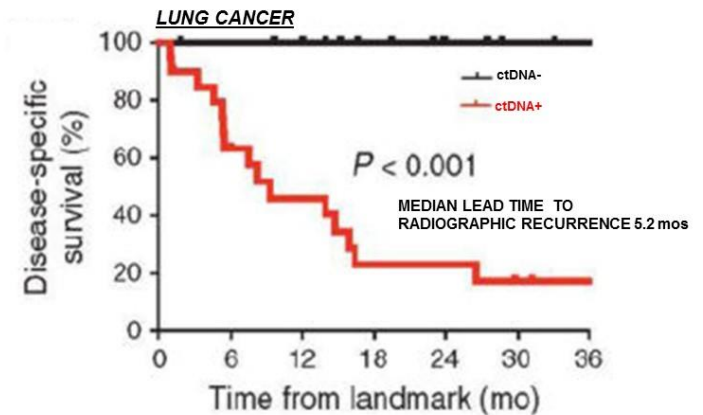
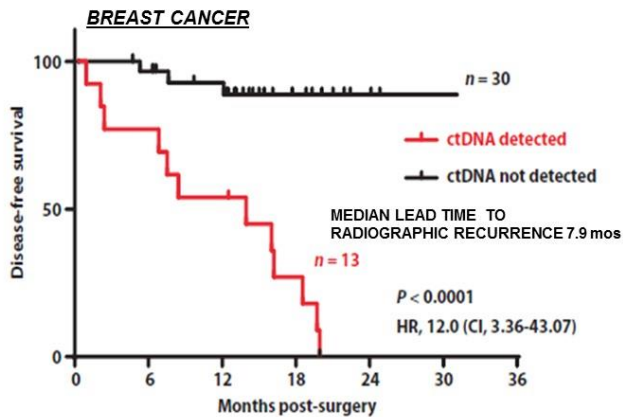
Novinky z ASCO GI 2020- nádory jícnu a žaludku

- Abstract 278: Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC). - Markus H. Moehler
- Abstract 282: Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study. - David Cunningham,
- **Biomarkers to Guide Surveillance and Adjuvant Therapy of Early-Stage Disease - Yelena Yuriy Janjigian**
- From Standardization to Personalized Care: How to Use Molecular Diagnostics to Guide Treatment - Harry H. Yoon

Biomarkers to Guide Surveillance and Adjuvant Therapy of Early-Stage Disease

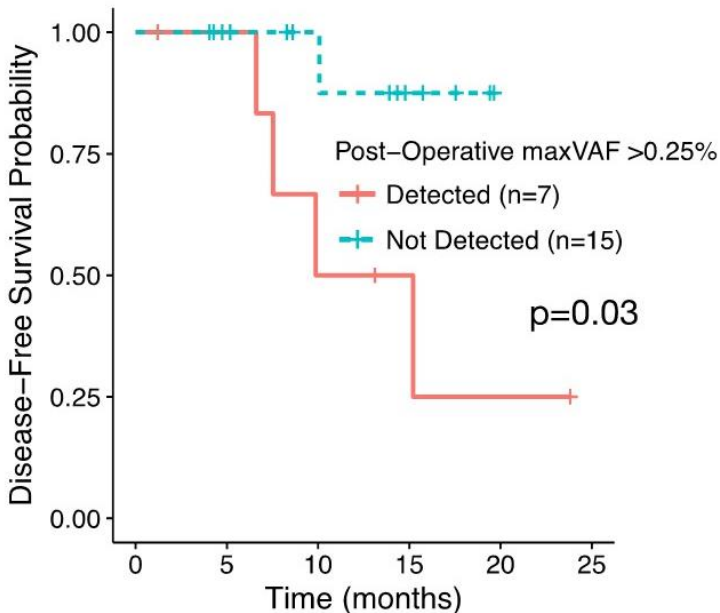
- Yelena Yuriy Janjigian

ctDNA POST-SURGERY PREDICTS RECURRENCE



ctDNA PREDICTS RECURRENCE IN GASTRIC CANCER

Within 6 months after surgery



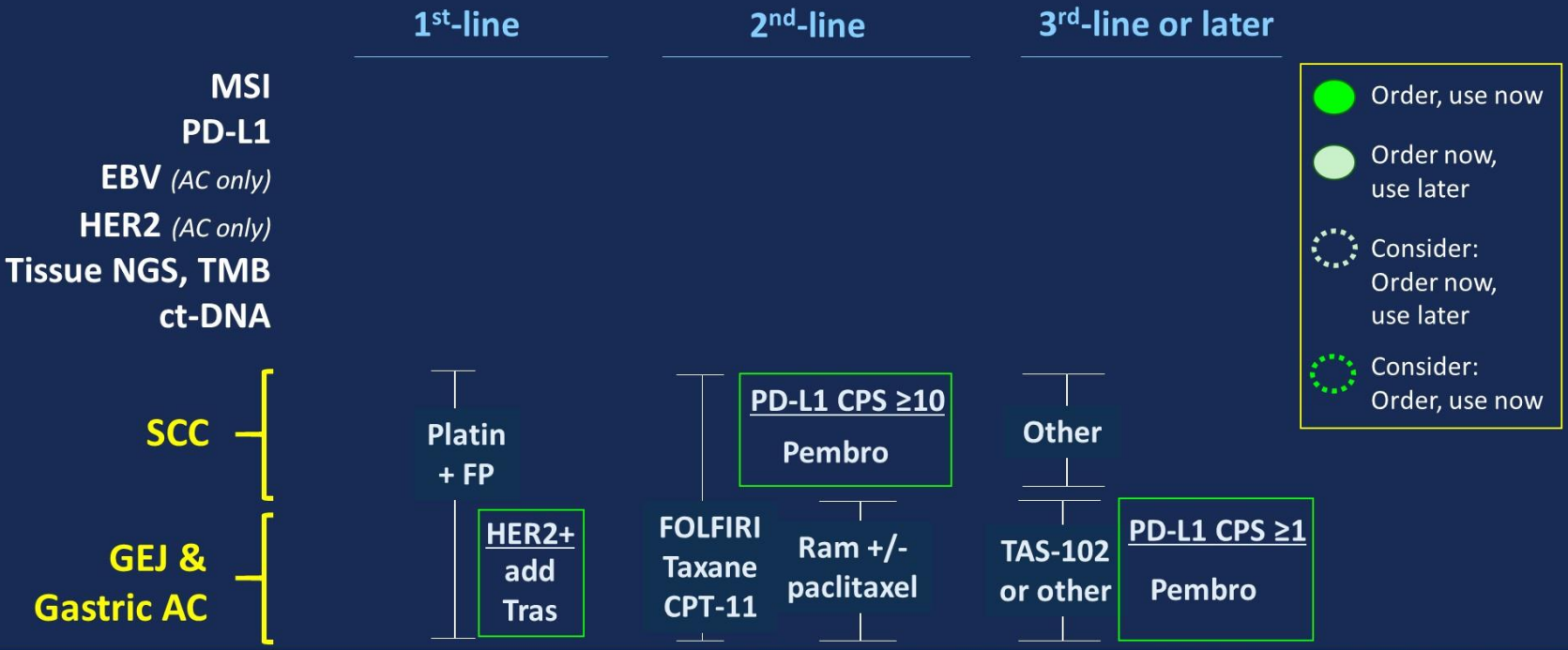
**Median mDFS
12.5 months vs. NR**

Novinky z ASCO GI 2020- nádory jícnu a žaludku

- Abstract 278: Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2– advanced gastric or gastroesophageal junction cancer (GC/GEJC). - Markus H. Moehler
- Abstract 282: Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study. - David Cunningham,
- Biomarkers to Guide Surveillance and Adjuvant Therapy of Early-Stage Disease - Yelena Yuriy Janjigian
- **From Standardization to Personalized Care: How to Use Molecular Diagnostics to Guide Treatment - Harry H. Yoon**

From Standardization to Personalized Care: How to Use Molecular Diagnostics to Guide Treatment - Harry H. Yoon

2020 one treatment & molecular approach for fit patient with advanced gastroesophageal carcinoma

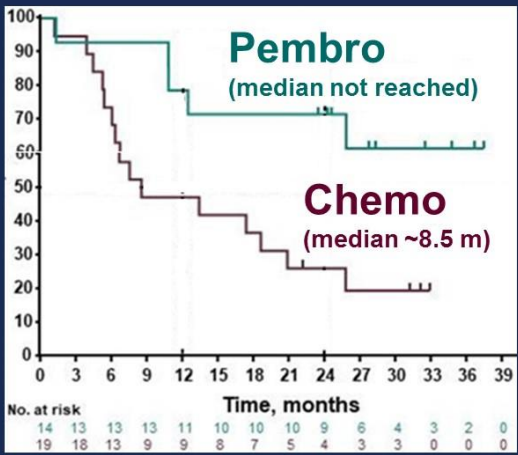


From Standardization to Personalized Care: How to Use Molecular Diagnostics to Guide Treatment - Harry H. Yoon

Pembro confers OS benefit in MSI gastric/GEJ adenoca in 1st line setting

Secondary analyses of phase III KN-062

1st-line (n = 23, all MSI-high)



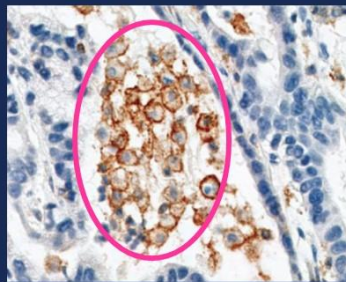
- HR 0.29 (95% CI 0.11 – 0.81)
- Duration of response on Pembro = 21.2 m

From Standardization to Personalized Care: How to Use Molecular Diagnostics to Guide Treatment - Harry H. Yoon

CPS (combined positive score), the only PD-L1 method predictive of immunotherapy benefit in gastroesoph cancer

$$\text{CPS} = \frac{\text{\# of } \textit{macrophages, lymphocytes}, \text{ or tumor cells that express PD-L1}}{\text{\# of tumor cells evaluated}} \times 100$$

In gastroesoph adenoca microenvironment, PD-L1 is expressed most commonly in immune cells (not tumor cells)



Take home message
Verify on path report that immune cells were counted.
If they were not, scoring must be repeated.

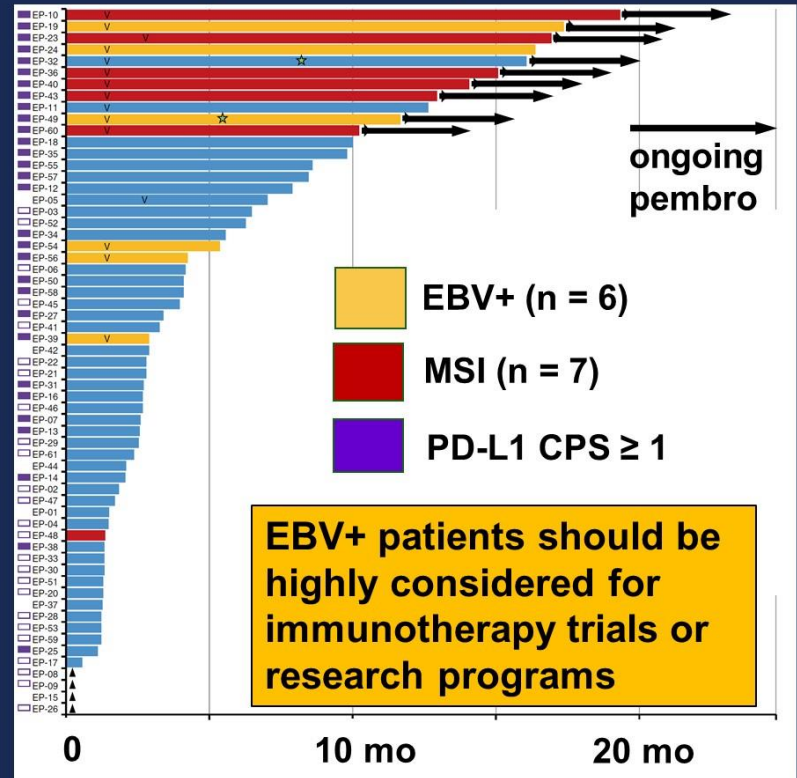
Inter-lab agreement for PD-L1 scoring (CPS 1 vs 0) is >90%

From Standardization to Personalized Care: How to Use Molecular Diagnostics to Guide Treatment - Harry H. Yoon

EBV+ gastric ca seems responsive to anti-PD-1 (comparable to MSI)

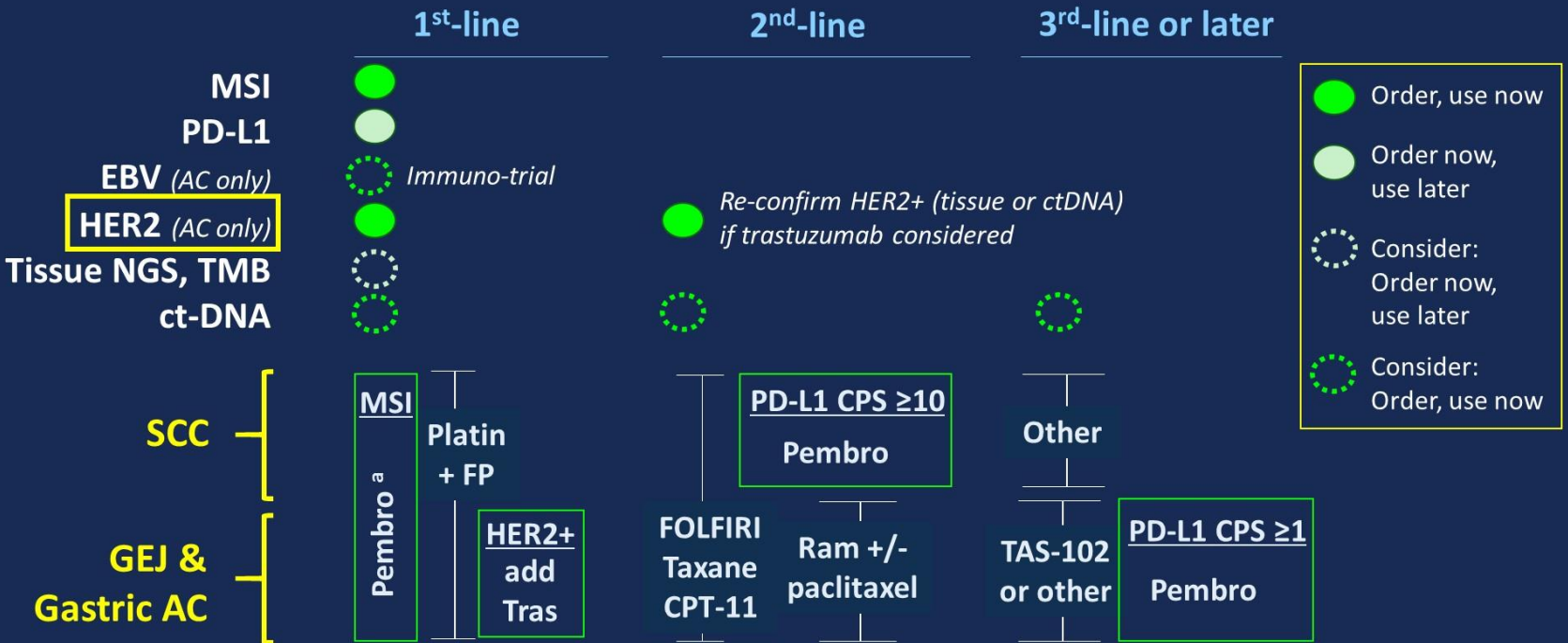
- All 6 (of 6) EBV+ patients had PR/CR with anti-PD-1 monotherapy
 - Response duration >10 mo in 3 patients
- Every EBV+ tumor was PD-L1 CPS ≥ 1
 - Usually NOT due to PD-L1 amp
 - Enriched with IFN gene signature
- PD-L1 CPS level in EBV+ tumor may not correlate response benefit
 - 3 longest responders: CPS 1, 5, 80
 - Other 3 patients had CPS 15 to 80

Advanced gastric cancer (N = 61) on pembro



From Standardization to Personalized Care: How to Use Molecular Diagnostics to Guide Treatment - Harry H. Yoon

2020 one treatment & molecular approach for fit patient with advanced gastroesophageal carcinoma



From Standardization to Personalized Care: How to Use Molecular Diagnostics to Guide Treatment - Harry H. Yoon

- MSI a PD-L1 před 1 linií
 - PD-L1 musí zahrnovat i bb imunitního systému
 - Využití i v 2. a 3. linii
- EBV+ využití pro stratifikaci pacientů do klinických studií s imunoterapií
- HER2 status znovu vyšetření po selhání léčby s HER2i



KEY

(pembro

TRU

lizumab)

DA[®]

Injection 100 mg

Learn more
KEYTRUDA.c

METRE

visit
our
exhibits
to learn
more
at
LEVIN

LEVIN

Děkuji za pozornost

