BRIDGE

Bridging knowledge in GI cancers

BRIDGE is an initiative by SERVIER that connects health care professionals worldwide, to share knowledge and unite actions for the benefit of GI cancer patients.

New evidence on 3L mGC, applied to daily practice

Webinar No 11
HIGHLIGHTS

Professor Sylvie Lorenzen

MD, PhD
Head of the Phase I Unit,
University Hospital rechts der Isar,
Technical University of Munich, Germany

Prof Lorenzen's research interests include clinical research in medical oncology, response evaluation in solid tumor therapy, and multimodality treatment of gastrointestinal cancer. She is head of the gastroesophageal working group of the Arbeitsgemeinschaft Internistische Onkologie (AIO).

Professor Aziz Zaanan

MD, PhD
Department of GI oncology
European Georges Pompidou Hospital,
University of Paris, France

Prof Zaanan is chairman of the French Gastrointestinal Oncologist Association, a member of the ESMO "Gastrointestinal tumors" faculty, and associate editor of *Clinics and Research in Hepatology and Gastroenterology*. His research focuses on the study of the genetic alterations in digestive tumors and their implications for prognosis and response to treatment.

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WEBINAR HIGHLIGHTS

GC is the 5th most common type of cancer worldwide **in terms of incidence,** and **the 4th cause of mortality** among cancers[1]

Eastern Asia and **Central/Eastern Europe** had the highest incidence and mortality rates in 2020[1]

One of the main objectives of 3L mGC treatments is to improve overall survival (OS) and progression-free survival (PFS) as well as prolongation of time to deterioration of ECOG PS≥2, QoL preservation, symptom control, and toxicity limitation* and to **allow further lines of treatments**

RECENT ADVANCES IN 1L MGC TREATMENT

1L chemotherapy + nivolumab

Improved OS in patients with PD-L1 CPS ≥5[2]
Was recently approved in the EU[3]
for PD-L1 CPS ≥5 adult patients with HER2-negative advanced or metastatic gastric cancer, GEJC, or EAC

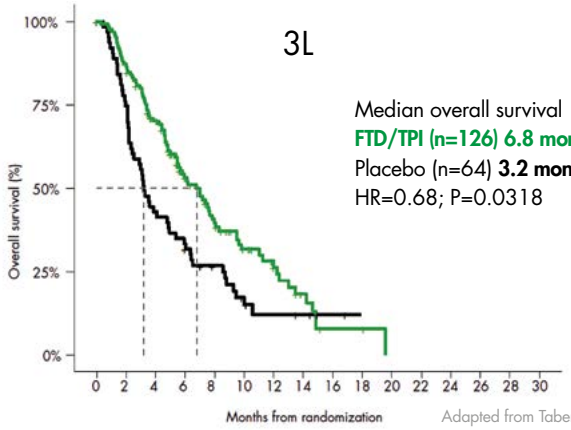
TAGS: THE ONLY GLOBAL PHASE III TRIAL IN 3L+ MGC

TAGS[4] is an international, randomized, double-blind, placebo-controlled, phase III trial, with 507 patients enrolled and randomly assigned: FTD/TPI + BSC (n=337) and placebo + BSC (n=170).

FTD/TPI provided a significant benefit in OS and PFS vs placebo[5]

With **superior benefits** when FTD/TPI was **admnistered in 3L vs 4L+[5†]**

OS:[4,5] 3L=6.8mo; 4L+=5.2mo; overall population=5.7mo



Adapted from Tabernero J et al, 2021[5]

TAGS is the only 3L+ mGC phase III study with QoL and PS outcomes[4]

QoL was maintained while on FTD/TPI[6], and was similar in **both 3L and 4L+ populations[5]**
>70% patients maintained an **ECOG PS of 0 or 1** at treatment end, making them **potentially eligible for subsequent therapies[5]**

FTD/TPI has mainly biological toxicities[4]

Specific AEs occurred at **similar rates in the 3L and 4L+** groups vs placebo[5]
No new safety concerns were noted in the GEJC subgroup vs GC[7]

IN CONCLUSION

- mGC tumor heterogeneity is a **major challenge** for effective targeted drug development
- Immune checkpoint therapy has efficacy, probably confined to distinct subgroups
- **In Europe FTD/TPI is the only approved and preferred 3L treatment** with clinically relevant OS improvement (+3.6 mo in 3L), and meaningful prolongation of median time to deterioration to ECOG PS ≥2 in 3L (+2.8 mo)

IMPACT ON THE DAILY PRACTICE

- In mGC, the aim is to prolong overall survival and therefore **sequential treatment strategy is a goal**
- FTD/TPI may provide potential de-escalation/ maintenance strategy and **"toxicity holiday"** (from classic platinum and taxane associated toxicities, such as neuropathy)» with a manageable safety profile, before reintroduction in later lines
- FTD/TPI might open the window for **reintroduction/ rechallenge strategy** like in CRC
- It offers the possibility to **benefit from treatments beyond 3L**

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for more details and watch the replay of the 18/11/2021 session

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for more details and watch the replay of the 24/11/2021 session

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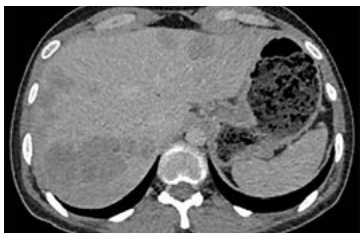
SUMMARY FROM THE INTERACTIVE CLINICAL CASE

Marc
Age: 65 years old
Gender: Male

Medical history: Grade 1 hypertension (no other medical history)
No smoking
Overweight: weight 90 kgs, height 180 cm (BMI=27.8 kg/m²)
Weight loss of ~5 kg in the past 6 months and slight epigastric discomfort
ECOG PS 0

Gastroscopy: ulcerated tumor in body of stomach
Biopsy: moderately differentiated adenocarcinoma
CT scan: multiple metastases in the lymph nodes, lung and liver

Molecular profile: HER2 negative, pMMR/MSS, PDL1 CPS 0



CT scan
Image provided by Prof Zaanan

May 2020
→ 1st line / Induction chemotherapy:
FOLFOX

After 2 months
Partial response

After 4 months
No disease progression
Growing neuropathy grade 2
STOP oxaliplatin
→ Only 5-FU

After 8 months
disease progression
No residual neuropathy
ECOG PS 1

Décembre 2020
→ 2nd line :
PACLITAXEL + RAMUCIRUMAB

After 2 months
Stable disease

After 4 months
March 2021
disease progression

April 2021
ECOG PS 1
Neuropathy grade 1
→ 3rd line:
FTD/TPI

After 2 months
Stable disease
Toxicity: nausea gr 1, neutropenia gr 2 and anemia gr 1 without reduction doses

After 4 months
disease progression‡
PS 1
No residual neuropathy

What would be your treatment option 4th line?

‡mPFS in the pivotal TAGS clinical study:[4,5]
3L=3.1mo; 4L+=1.9mo; overall population=2.0mo

Based on Pr Zaanan's clinical experience

FTD/TPI ENABLES FURTHER-LINE THERAPY TO EXTEND PATIENTS' CONTINUUM OF CARE

Results from polls

What would you give in 3rd line?

In 3L, most physicians would choose FTD/FTI§

What would you give in 4th line , after choosing FTD/TPI in 3rd line?

Best supportive care	0%
Irinotecan	33.3%
Nivolumab	15.6%
Other	2.2%
Reinduction with FOLFOX	48.9%

§ FTD/TPI: 88.9% ; Nivolumab: 4.4% ; BSC: 4.4% ; Other: 2.3%

These results reflect the votes of the audience that attended the live webinar sessions and do not reflect Servier's view or the PIs. Please always refer to your relevant PIs and regulatory compliance. The audience included a total of 107 physicians from 24 countries.

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INSIGHTS FROM THE EXPERT'S CLINICAL PRACTICE*

"It's important to give FTD/TPI at a stage where the patient is still in a good condition. The effect of FTD/TPI is more profound in 3L compared with further lines; there's a longer progression-free survival and a longer time to the deterioration of ECOG PS ≥2."

"The more lines the patient is given, the more important quality of life becomes. With 3L FTD/TPI, we maintain quality of life by controlling the disease."

"In the TAGS study, more than 2 out of 3 patients were still in a good condition status with a good quality of life at the end of the treatment. It's very important because we will be able to offer those patients a further line of chemotherapy and discuss the reintroduction of FOLFOX, or Irinotecan."

CLICK HERE for more details and watch the replay of the 18/11/2021 session

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1L: first line; 2L: second line; 3L: third line; 4L: fourth line; AE: adverse event; BMI: body mass index; BSC: best supportive care; CI: confidence interval; CPS: combined positive score; CRC: colorectal cancer; CT: computerized tomography; DCR: disease control rate; dMMR: deficient mismatch repair; EAC: esophageal adenocarcinoma; ECOG: Eastern Cooperative Oncology Group; ESMO: European Society of Medical Oncology; EU: European Union; FOLFOX: 5-fluorouracil + oxaliplatin; FP: fluoropyrimidine; FTD/TPI: trifluridine/tipiracil; GC: gastric cancer; GEJC: gastroesophageal junction cancer; gr: grade; HER2: human epidermal growth factor receptor-2; HR: hazard ratio; JSMO: Japanese Society of Medical Oncology; mGC: metastatic gastric cancer; mo: months; MSS: microsatellite stable; ORR: objective response rate; OS: overall survival; PD-1: programmed cell death-1; PD-L1: programmed death-ligand 1; pMMR: proficient mismatch repair; PS: performance status; pts: patients; QoL: quality of life; US: United States.

TAGS: NCT02500043

*** Based on presenter's clinical experience; †Unplanned exploratory subgroup analysis of the TAGS study.**

References:

1. Globocan 2020 - Stomach. Available at: https://gco.iarc.fr/today/data/factsheets/cancers/7-Stomach-fact-sheet.pdf. Accessed: March 2022. 2. Janjigian YY et al. First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial. Lancet. 2021; 398(10294):27–40. 3. Nivolumab Professional information – www.swissmedicinfo.ch. 4. Shitara K et al. Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2018; 19(11):1437-1448. 5. Tabernero J et al. Trifluridine/tipiracil versus placebo for third or later lines of treatment in metastatic gastric cancer: an exploratory subgroup analysis from the TAGS study. ESMO Open. 2021;6(4):100200. 6. Tabernero J et al. Health-related quality of life associated with trifluridine/tipiracil in heavily pretreated metastatic gastric cancer: results from TAGS. Gastric Cancer. 2020;23:689-698. 7. Mansoor W et al. Trifluridine/tipiracil in patients with metastatic gastroesophageal junction cancer: a subgroup analysis from the phase 3 TAGS study. Gastric Cancer. 2021; 24:970–977.

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Available on replay

Third-line therapy in mCRC live conference
Prof Julien Taieb

Continuum of care in mPaCa live conference
Prof Gerald Prager

Treating mPaCa patients: from scientific evidence to real clinical practice
Prof Teresa Macarulla

Addressing the unmet needs in 3L mGC: a clinical perspective
Prof Sylvie Lorenzen & Dr Elizabeth Smyth

mPaCa clinical cases: experience sharing from Asia and Europe
Prof Junji Furuse & Prof Ivan Vilmos Borbath

Maximizing benefit for patients in 3L mCRC, clinical case discussion
Prof Timothy Price

Bridge season 1

Management of mPaCa patients in Asia: what are the specific features compared with the rest of the world?
Prof Changhoon Yoo

Challenges in the management of GI cancer, a clinical perspective on 3L mCRC & mGC
Prof Florian Lordick& Prof Pia Österlund

Where do we stand in mPaCa?
Prof Thomas Seufferlein

New evidence on 3L mGC, applied to daily practice
Prof Sylvie Lorenzen & Prof Aziz Zaanan

Treatment strategy in mPaCa: Extending the continuum of care
Prof Gerald Prager

REPLAY **CLICK HERE** to find all sessions available on replay

Upcoming webinar

Extending the continuum of care in 3L mCRC: from scientific evidence to daily clinical practice

Prof Chiara Cremolini
MD, PhD
Associate Professor in Medical Oncology, University of Pisa, Italy

Thursday April 26, 2022
5:30 PM CET
CLICK HERE to register

Dr Anelisa K. Coutinho
MD
Clinical oncologist and coordinator of the Gastrointestinal Tumors department, Cilnica AMO of Salvador, Brazil

Thursday April 28, 2022
7 PM CET
CLICK HERE to register

LONSURF® is indicated for the treatment of adult patients with metastatic colorectal cancer who have been previously treated with available including fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and anti EGFR agents in patients with non-mutated KRAS status (wild type). Gastric cancer: Treatment of adult patients with metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction. Patients must have been previously treated with at least two fluoropyrimidine-, platin- and taxane- or irinotecan-based chemotherapies and if appropriate with a targeted HER2/neu treatment.*

*For more information, please consult the professional information at: www.swissmedicinfo.ch/

Servier (Switzerland) S.A., La Voie Creuse 16, 1202 Genève

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