BRIDGE

Bridging knowledge in GI cancers

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

Maximizing the benefit for patients in 3L mCRC:

Clinical case discussion

Webinar No 6
HIGHLIGHTS

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Prof Timothy Price is Senior Consultant Medical Oncologist and Director of Medical Oncology and Clinical Cancer Research at The Queen Elizabeth Hospital in Adelaide. His major clinical interest is in treatment of patients with gastrointestinal cancer, and he is currently involved in an extensive gastrointestinal clinical trial program. He is professor at the University of Adelaide and Colorectal Cancer Stream leader for the South Australian Health and Medical Research Institute, and leads the gastrointestinal translational and research laboratory at the Basil Hetzel Institute. He chairs the current national NHMRC Cancer Council Colorectal Guidelines committee which led to the recently published update. He is also a visiting/honorary professor at the University of Sydney and the University of Antwerp.

SERVIER

WEBINAR HIGHLIGHTS

CRC is the 2nd most commonly diagnosed cancer, in Europe and a leading cause of death, both in Europe and worldwide[1]

Compared with 20 years ago, mOS of mCRC patients has doubled and is now **~30 months**

Therapeutic sequencing is key in the continuum of care*, 2, 3

Objectives in 3rd line are **treatment efficacy, safety/tolerance,** and **QoL maintenance** to allow further treatments afterwards*

IN THE RECOURSE TRIAL

International, randomized, double-blind, placebo-controlled, phase 3 trial conducted in 4 main regions (Japan, US, Europe, and Australia), with 800 total patients enrolled.**, 4

Exploratory analysis by prognostic factors[5]

GOOD prognostic characteristics (GPC n=386)[5]

Low tumor burden/less aggressive disease
1 or 2 met sites AND time since 1st met diagnosis ≥18 mo

BEST prognostic characteristics (BPC n=153)[5]
Good prognostic characteristics
NO LIVER METASTASES

POOR prognostic characteristics (PPC n=414)[5]

High tumor burden/aggressive disease
≥3 met sites AND/OR time since 1st met diagnosis <18 mo

Adapted from Tabernero *et al*, 2020[5]

mOS in months	FTD/TPI	Placebo
BPC (n=153)	16.4	8.6
GPC (n=386)	9.3	6.8
PPC (n=414)	5.3	4.4

mPFS in months	FTD/TPI	Placebo
BPC (n=153)	5.4	1.9
GPC (n=386)	3.3	1.8
PPC (n=414)	1.9	1.7

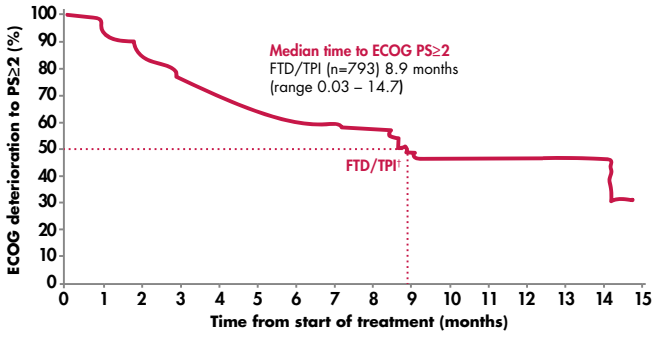
Treatment with FTD/TPI improved OS in all prespecified subgroups[4]

IN THE PRECONNECT TRIAL

Ongoing, international, multicenter, open-label, single-arm, phase 3b study done in 13 countries, with 793 total patients enrolled (71 from Australia). Same inclusion and exclusion criteria as those in the RECOURSE trial.***, 7

- **Neutropenia grade ≥3** was experienced by 39% of patients in PRECONNECT and 38% in RECOURSE[7]
- **Febrile neutropenia** was experienced by 1.4% of patients in PRECONNECT and 4% in RECOURSE[7]
- **Patients' QoL was maintained** throughout the trial[7]
- **In Australia,** FTD/TPI was more likely to be introduced earlier on, compared with the global cohort[8]

FTD/TPI has an acceptable safety profile[7]



Adapted from Bachet *et al*, 2020[7]

79.8% of patients maintained an ECOG PS of 0 or 1 at treatment end, making them potentially eligible for subsequent therapies[7]

IN A RETROSPECTIVE, LONGITUDINAL COHORT STUDY

Evaluation of treatment adherence to FTD/TPI and regorafenib in a "real-world" setting, from analysis of a US database (N=3055)[9]

With regorafenib	With FTD/TPI
78% of patients **discontinued** at 6 months[9]	**62%** of patients **discontinued** at 6 months[9]

P<0.001

Adapted from Patel *et al*, 2018[9]

The proportion of patients who discontinued therapy was higher with regorafenib treatment[9]

In conclusion, for third-line mCRC:

- **For the majority, FTD/TPI and regorafenib are the standard of care based on phase 3 trials*, 4, 7**
- **Tolerance and patient factors are used in the clinic to decide on best options*, 7, 9**
- **Therapeutic sequencing is key in the continuum of care*, 2, 3**

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REPLAY **CLICK HERE** for more details and watch the replay of the 22/04/2021 session

BRIDGE GI cancers

SUMMARY FROM THE INTERACTIVE CLINICAL CASE

Age: 73 years old
Gender: male
Symptomatic rectal cancer
Lung metastasis
MSS, RAS MT adenocarcinoma
ECOG PS 1

Provided by Prof Price

July 2018
- After "watch and wait" for 6 months, had cough and ongoing progression

→ Started 1st line:
capecitabine/oxaliplatin + anti-VEGF (bevacizumab)

December 2018
- Tolerated the treatment poorly and had minor response

→ Stopped after 5 months due to tolerance

July 2019
- Monitoring revealed lung progression

→ Started 2nd line:
irinotecan + anti-VEGF (bevacizumab)
- Grade 2 diarrhea and neutropenia

→ Dose interruptions/adjustments

March 2020
- CT revealed partial response, treatment continued for 8 months
- Then stable CT

→ Decided to stop

July 2020
- MRI after collapse: reveals cerebellar lesion
- Lung and primary are stable
- Resection and radiotherapy

September 2020
- MRI brain: clear
- Lung disease progression with minor cough

→ Started 3rd line
FTD/TPI

Based on presenter's clinical experience

RESULTS FROM POLLS

What would you give in 1st line?

Capecitabine/oxaliplatin + anti-VEGF	40%
FOLFIRI + anti-VEGF	29%
FOLFOX + anti-VEGF	31%
No treatment	0%

What would you give in 3rd line?

FTD/TPI	80%
Irinotecan-based treatment	3%
Oxaliplatin-based treatment	2%
Palliative care referral	2%
Regorafenib	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 was a total of 94 physicians from 38 countries

INSIGHTS FROM THE EXPERT'S CLINICAL PRACTICE

"A patient with only one or two metastatic sites and for whom time since diagnosis is greater than 18 months fits into the good prognostic population. In the case presented, this is what I considered to choose the third line of treatment. The patient responded and probably did well partly because of these factors."

"A patient with RAS wildtype, low tumor burden, and slow disease progression, would have probably had doublet chemotherapy with anti-EGFR as first-line therapy. Reintroduction or rechallenge with anti-EGFR drugs may be something to consider in third line, but it would depend on whether he failed it or whether he'd stopped and started because of tolerance."

"Sarcopenia is something we will increasingly look at throughout the lines of therapy to help us select patients in the research setting."

"If we get to the third-line space in patients with a high-volume disease, a good response in first line with platinum, and probably a better disease control, I think FTD/TPI at that point is still a reasonable option. If you've got a very bulky disease, you might consider going back to the platinum if they'd had a really good response. It's a difficult clinical situation depending on the patient, but I still think FTD/TPI is an option in that space because of its tolerance and ability to stabilize diseases."

"Data show that the rate of neutropenia is relatively high, but importantly the rate of febrile neutropenia is actually quite low. We do have G-CSF for example to control that. So in my own practice, it's quite a straightforward problem to manage."

"Unusual sites, particularly bone, often reflect BRAF mutation. In that setting, you may think to assess the new targeted encorafenib and cetuximab, for example, maybe prior to then going on to FTD/TPI. The molecular profile may guide you more rather than necessarily where that disease is."

"FTD/TPI is working well for the patient shown. As a possible next line of active treatment, perhaps going back to either systemic chemotherapy option may be reasonable, although single agent irinotecan probably is a good option."

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BSC: best supportive care; CRC: colorectal cancer; CT: computerized tomography; ECOG PS: Eastern Cooperative Oncology Group performance status; EGFR: epidermal growth factor receptor; FTD/TPI: trifluridine/tipiracil; HR: hazard ratio; met: metastasis; mCRC: metastatic colorectal cancer; mo: months; mOS: median overall survival; MRI: magnetic resonance imaging; MSS: microsatellite stable; MT: mutation; OS: overall survival; QoL: quality of life; US: United States; VEGF: vascular endothelial growth factor; WT: wild-type

* Based on presenter's clinical experience; ** Patients with biopsy-documented metastatic adenocarcinoma of the colon or rectum, and knowledge of KRAS tumor status (ie, wild-type or mutant), who had received at least two previous chemotherapy regimens with each of the following agents: a fluoropyrimidine, oxaliplatin, irinotecan, bevacizumab, and — for patients with KRAS wt tumors — cetuximab or panitumumab, were eligible. Patients had to be ≥ 18 years old; have adequate bone-marrow, liver, and renal function; and an ECOG PS status ≤ 2. Patients received either BSC plus oral FTD/TPI (35 mg/m^2 2x daily, 5 days a week, with 2 days of rest, for 2 weeks, followed by a 14-day rest period, repeated every 4 weeks), or BSC plus placebo; *** Patients received oral FTD/TDI 35 mg/m^2 twice daily on days 1–5 and 8–12 of each 28-day cycle; †Although baseline ECOG PS data were not collected for 24 patients, data were collected at subsequent visits, so these patients were included in the analysis.

References:

1.Taieb J *et al. Ann Oncol.*2017;28(4):824-830; 2.Yoshino T *et al. Ann Oncol.*2018;29(1):44-70; 3.Van Cutsem E *et al. Ann Oncol.*2016.27(1):1386-1422; 4.Mayer RJ *et al. N Engl J Med.* 2015;372:1909–1919; 5.Tabernero J *et al. ESMO Open.*2020;5:e000752; 6.Van Cutsem E *et al. Eur J Cancer.* 2018;90:63–72; 7.Bachet J *et al. ESMO Open.* 2020;5(3):e000698; 8.Price JT *et al. Ann Oncol* (2020) 31 (suppl_6): S1273-S1286. 10.1016/annonc/annonc355.107P (Poster); 9.Patel AK *et al. Clin Colorectal Cancer.*2018;17:e531–e539.

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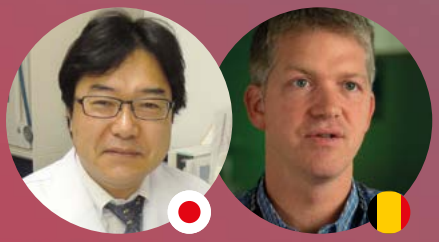
Available on replay

Third-line therapy in mCRC live conference
Prof Julien Taieb

Continuum of care in mPaCa live conference
Prof Gerard 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

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

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Upcoming webinars

Challenges in the management of GI cancer, a clinical perspective on 3L mCRC & mG

Prof Florian Lordick
Professor of oncology, Leipzig University, Germany
Director of the department of oncology, Leipzig University Medical Center, Germany

Monday June 21, 2021
7.00 PM CEST
CLICK HERE to register

Prof Pia Österlund
Adjunct professor, Karolinska Institutet, Sweden
Deputy head of the oncology department, Tampere University Hospital, Finland

Wednesday June 23, 2021
3.00 PM CEST
CLICK HERE to register

Where do we stand in mPaCa?

Prof Thomas Seufferlein
Medical Director at the Clinic for Internal Medicine I, University Hospital Ulm, Germany

Wednesday July 7, 2021
7 PM CEST
CLICK HERE to register

Thursday July 8, 2021
12 PM CEST
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LONSURF® indication:
As monotherapy for the treatment of adult patients with metastatic colorectal cancer who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGFR agents.
As monotherapy for the treatment of adult patients with metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction, who have been previously treated with at least two prior systemic treatment regimens for advanced disease.*

*For more information, please consult the abridged Summary of Product Characteristics available here.
Prepared by headquarters in accordance with the International Reference Product Information approved on 12/2020.
Confidential – To be adapted and approved at local level prior to local use.

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