

GUIDE

COMMUNICATION FRAMEWORK

Supported By



INTRODUCTION

- Our Scientific Committee consisting of Nina Grenon, Sven De Keersmaecker and Fransen McGinley developed **GUIDE**, on behalf of the GI NURSES CONNECT group
- GUIDE is a **communication framework** that will help you have even better conversations with your patients, to educate and guide them throughout their cancer treatment journey
 - These conversations will make it easier to educate, guide and empower your patients in the shared treatment decision
- While GUIDE aims to improve the benefit of interactions between nurses and patients with **colorectal cancer (CRC)**, the principles can be more **widely applied** to interactions with patients with **any other cancer**
- This programme is primarily aimed at **gastrointestinal (GI) oncology nurses and advanced practice providers** around the world. We will refer to both groups using the word 'Nurse'

INTRODUCING THE **SCIENTIFIC COMMITTEE**



NINA GRENON, DNP, AGCNP-BC, AOCN
Nurse Practitioner

- Nurse Practitioner caring for patients with Gastrointestinal Cancers for 22 years
- Adjunct faculty at Simmons College, School of Nursing and Health Sciences
- Clinical preceptor for nurse practitioner students at Yale University, Simmons College and MGH Institute of Health Professions
- Member of the North America Neuroendocrine Association Tumor Society, regional education committee
- Member of the Oncology Nursing Society



SVEN DE KEERMAECKER, RN
Oncology Nurse

- Study Coordinator since 2015, caring for study patients and outpatients
- 3 years of experience as a nurse in Intensive Care
- Oncology Nurse since 2000
- Acted as a nurse navigator in digestive oncology
- Involved in the development of coaching programs and health informatics tools
- Member of the European Oncology Nursing Society



FRANSEN MCGINLEY, MHS, PA-C
Physician Assistant

- Certified Physician Assistant caring for patients with gastrointestinal cancers for over 12 years
- Bachelor's degree in Microbiology from the University of Oklahoma
- Master's degree from the University of Oklahoma Health Sciences Physician Associate Program
- Active member of the National Commission on Certification of Physician Assistants
- Active member of the Oklahoma Academy of Physician Assistants

WHAT WILL YOU LEARN?

- 1** **Know** the required information to empower patients treated for colorectal cancer (CRC) and be able to respond to a fully comprehensive range of questions
- 2** **Know and explain** those aspects of CRC and its treatment that are essential for the patient to understand, including effective management of side effects
- 3** **Know how** to have supportive relationships with patients to enhance understanding and ultimately drive adherence
- 4** **Know how** to apply the recommended framework across a variety of interactions to strengthen shared decision-making and deliver the best possible patient care



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7. SUMMARY & CLOSE

INTRODUCING GUIDE

- This e-learning programme **aims to support nurses in their role as a go-to figure for their patients**, being an active member of the multidisciplinary team (MDT) in delivering shared decision-making, empowering and educating patients to communicate about their disease and treatment
- **GUIDE's five letters** each represent a crucial step in your conversations with patients with CRC
 - **G**: Gain insight into the goals of treatment and care
 - **U**: Understand the gaps in the patient's knowledge
 - **I**: Inform and Educate
 - **D**: Direct to additional support
 - **E**: Empower the patient
- In each step, we will address:
 - What you need to **know**
 - What to **explain** to the patient
 - How best to **educate** the patient
- You will notice GUIDE is a **flexible approach**
 - You will develop your own preferences with regards to how many steps you move through in the first appointment with the patient and how you approach the subsequent steps, face-to-face or over the telephone
 - This will vary from patient to patient, depending on their individual circumstances, such as their capacity to absorb additional information and the presence of the carer

INTRODUCING **GUIDE**

GUIDE's five letters each represent a crucial step in your conversations with patients with CRC.

Gain insight into the goals of treatment and care

G

Understand the gaps in the patient's knowledge

U

Inform and Educate

I

Direct to additional support

D

Empower the patient

E

In each step, we will address:

- What you need to **know**
- What to **explain** to the patient
- **How** best to educate the patient

PRINCIPLES AND USE OF THE **GUIDE** COMMUNICATION FRAMEWORK

PRINCIPLES OF **GUIDE**

- ✓ **GUIDE** aims to support nurses in their role as a go-to figure for their patients
- ✓ The ultimate goal is to improve patient outcomes through enhanced patient engagement, understanding and outlook
- ✓ The framework may be delivered over several interactions and should be adapted to meet the patient's needs
- ✓ The role of the carer should also be considered, so they feel engaged appropriately

HOW COULD YOU USE **GUIDE**?

- ✓ Include each step into your conversations with patients with CRC
- ✓ Consider the need to incorporate the framework over a series of consultations
- ✓ Apply the principles to communication with family or carers
- ✓ Use **GUIDE** in conversations with patients with other types of cancers
- ✓ Encourage your team to complete this training and follow the steps consistently

INTRODUCING **SANDRA JENSEN**



SANDRA JENSEN
Patient with CRC

*Fictional patient case

- In this educational programme, we will focus on **Sandra Jensen**, a 51-year old patient with Stage IV, KRAS/NRAS-wild type rectal cancer*
 - Her **disease progressed** with liver metastases 16 months after total resection and adjuvant chemotherapy for metastatic disease
 - She has received
 - First-line FOLFOX + cetuximab
 - Second-line FOLFIRI + bevacizumab
- Oncologist Dr. Paul Ross has just told Sandra her disease progressed on the current treatment. He has proposed **third-line treatment with regorafenib**
- Sandra came to the visit alone and did not expect the news Dr. Ross has just given her
- **Nurse Ann Garcia will now sit down with Sandra** to further discuss her treatment and care

STEP 1

G

**GAIN INSIGHT INTO THE GOALS
OF TREATMENT AND CARE**

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LEARNING OBJECTIVE

GAIN INSIGHT INTO THE GOALS OF TREATMENT AND CARE

WHAT

WILL YOU LEARN?

In this section you will learn all about the **need to gain insight into the goals of treatment and care** as a first step in supporting your patient along the agreed treatment journey

WHY

IS THIS IMPORTANT?

Being part of the team that makes the treatment decision will allow you to **fully understand and support it**, instilling confidence in your patient

THE RIGHT KNOWLEDGE

Before engaging in a conversation with a patient, it is essential for the nurse to know

- The **goals of treatment and care** for this patient
 - Which **treatment is prescribed** to this patient and the **rationale** for it
-
- Adopting a **proactive approach** and being actively involved in the MDT is key to obtain the information you need
 - Being part of the team that makes the treatment decision will allow you to fully understand and support it
 - This will allow you to accurately inform the patient and provide patient-centred care
 - Despite a high-quality relationship between the patient and the oncologist, it is often the nurse who the patient will feel more comfortable with discussing their treatment, side effects, symptoms and wider issues

Practical tip:

Beyond the medical goal of treatment (e.g. disease control), it is often helpful for patients to have an achievable short-term goal, like attending a wedding or the birth of a grandchild.

WHAT NEEDS TO BE EXPLAINED TO THE PATIENT

INITIAL ENGAGEMENT

- **Appreciating the patient's understanding and wishes** will set the course of the nurse-patient relationship
 - Some patients like to be informed in detail (including e.g. specific laboratory values, extent of tumour burden) to be able to actively participate in the treatment decision. Others can easily be overwhelmed by too many details
- **Find the right balance** for each individual patient

Questions you may want to ask your patient at this stage:

- What is your understanding where you are in your illness?
- How much information about what may be ahead would you like?



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THE RIGHT WAY TO DELIVER THE MESSAGES

- Reiterate the treatment decision is a **shared decision**, underlining that the patient has choices
- Talk to the patient with **reassurance and confidence**
 - Being fully informed on the goals of treatment and care for this patient, the treatment plan and the rationale will allow you to do this
- Allow room for the patient's **feelings and emotions**
- This approach will make the patient feel you are **the knowledgeable go-to person** they can rely on throughout the journey

Practical tip:

Actively advise patients that you can give them as much or as little information as they would like. For example: “are you a person who likes everything explained in detail or would you prefer me to summarise for you?”

Practical tip:

Repeat the patient's personal treatment goal back to them, to demonstrate that you understand the theoretical as well as the personal treatment goal that they are aiming for.

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STEP 1

SUMMARY

GAIN INSIGHT INTO THE GOALS OF TREATMENT AND CARE

DO

- Demonstrate to the patient that you fully understand and support the goals of treatment and care, the treatment prescribed and the rationale for it
- Understand the right level of detail for each individual patient
- Talk to the patient with reassurance and confidence
- Emphasise the positives without ignoring the negatives
- Be sensitive to the patient's emotions



AVOID

- Lacking involvement and proactivity in the MDT
- Being unaware of the treatment plan, the treatment rationale or the goal of treatment and care
- Focusing on negative news
- Holding back information, assuming the patient does not want to know
- Overwhelming patients with details, not respecting emotions



STEP 2

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**UNDERSTAND THE GAPS IN THE
PATIENT'S KNOWLEDGE**

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LEARNING OBJECTIVE

UNDERSTAND THE GAPS IN THE PATIENT'S KNOWLEDGE

WHAT

WILL YOU LEARN?

In this section you will learn all about **understanding the gaps** in the patient's knowledge, allowing you to prioritise where you focus when it comes to informing and educating the patient

WHY

IS THIS IMPORTANT?

Understanding the gaps allows you to prioritise where you focus, increasing efficiency

Knowledge gaps can be detected and addressed using the **Ask, Tell, Ask** model

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THE RIGHT KNOWLEDGE

- The level of knowledge and understanding of the disease and its impact and treatment **varies from patient to patient**
- By understanding misconceptions and gaps in the patient's knowledge, you can **efficiently educate** the patient
 - This understanding is powerful in **establishing a trusting relationship** with the patient
- The **carer** can play a key role in increasing understanding
 - The carer can **help you reach the patient's knowledge gaps** more quickly. Carers can provide a different perspective and perhaps a truth that the patient does not want to admit to
 - Understanding and addressing the **carer's knowledge gaps** as well, allows you to assist the patient's understanding

THE RIGHT KNOWLEDGE

ASK, TELL, ASK

- Use the **Ask, Tell, Ask (ATA)** model to discover knowledge gaps and efficiently educate patients

Ask the patient to describe their understanding to you, so you can build on their current knowledge level

Tell the patient the right information to fill their knowledge gaps

Ask the patient to explain the information back to you in their own words, so you can confirm they have understood your main messages

Practical tips:

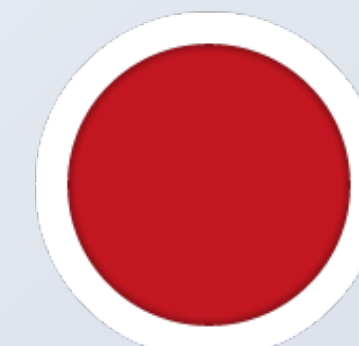
Using the word 'why' is a great way to gather greater depth of insight. For example: "Do you know why you are taking this treatment?" Keep asking 'why' following a patient response until you feel you have got to the crux of the patient's level of understanding.



ASK



TELL



ASK

In **Step 2** of the **GUIDE** framework, we focus on **Ask**

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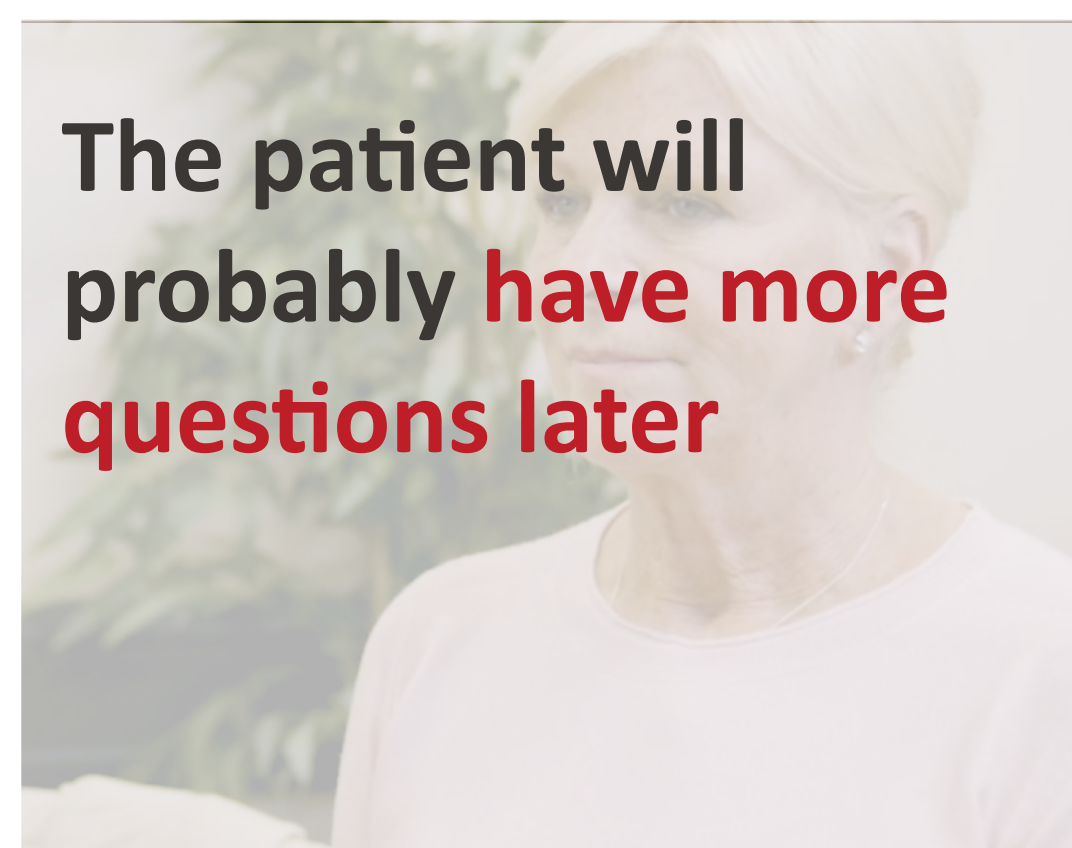
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WHAT NEEDS TO BE EXPLAINED TO THE **PATIENT**

- It is important that the patient **understands** some of the **fundamentals** of the treatment
 - The treatment aim
 - How the drug works
 - Why this specific drug was prescribed
 - Potential side effects and how to manage them



The patient will probably **have more questions later**

The Patient



The nurse is always **there for the patient** as a supporter, navigator and guide throughout the cancer journey

The Nurse



Carers are very important every step of the way

The Carer

Practical tip:

Advise patients to write down their questions and call or bring them to the next appointment. Emphasise that all questions are good questions.

Practical tip:

Advise patients to always have 'a second pair of ears' with them. Two hear more than one.

THE RIGHT WAY TO DELIVER THE MESSAGES

- Emphasise that by **understanding the treatment fundamentals**, the treatment journey will be smoother
- Ask **questions** in a way that reinforces you are doing so in order **to support** the patient and **not 'test'** them
- Discussing the gaps in the patient's understanding with **openness and empathy** will allow you to inform and educate the patient with **reassurance and confidence**
 - This will make the patient feel you are the knowledgeable go-to person they can rely on throughout the journey
- Encourage patients to **bring someone with them** to the next appointment
 - A carer can help increase understanding, but may also have his/her own questions and perspective

Practical tip:

It can be difficult for patients to say they do not understand, especially when they are already feeling vulnerable. Asking to explain the information given back to you in their own words is a nice way to work around this.

THE RIGHT WAY TO DELIVER THE MESSAGES

PHONE CONVERSATIONS

Telephone calls are **increasingly important** in cancer care, reaching out to patients before issues arise.

Tips and tricks for efficient phone conversations with patients:



Prepare for the conversation by reviewing the patient's status and treatment plan in advance



Take the time for the phone conversation, avoid distraction



Use the Ask, Tell, Ask model



Listen carefully without jumping to conclusions



As visual cues and body language are absent, rely not only on verbal but also on non-verbal clues, like shortness of breath or hesitancy in answering a question



Allow patients time to ask questions

THE RIGHT WAY TO DELIVER THE MESSAGES

PHONE CONVERSATIONS

Suggestions for questions to ask in phone conversations. Pick from this list the questions applying to the GUIDE step you are in.

GENERAL WELL-BEING AND ADVERSE EVENTS (AEs)

- How are things going with the treatment?
- List the potential side effects and ask if the patient is experiencing any or all,
 - including diarrhoea, nausea, hand-foot skin reaction (HFSR) and mouth sores
- Are you tired? And is it the same as before, better or worse?
- Are you getting out? What are you doing during the day?
- How is your appetite? Are you able to drink and stay hydrated?
- Are you having any pain?
- How is your mood?

ADHERENCE

- Can you tell me the name of the medication you are using?
- How often do you take your medication?
- Do you take medication with or without food?
- How do you store your medication?
- Do you have trouble swallowing the medication?
- Have you missed any doses or vomited after a dose?
- Were you able to read and understand the prescribing information?

STAYING IN CONTACT

- Do you know when to contact us? When is that?
- Do you know how to contact us? How is that?

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STEP 2

SUMMARY

UNDERSTAND THE GAPS IN THE PATIENT'S KNOWLEDGE

DO

- Use the 'Ask, Tell, Ask' model to discover knowledge gaps and efficiently educate patients
- Active listening
- Consider the role of the carer
- Allow time for questions and take the time to answer them
- Encourage patients to write down their questions for the next appointment or call
- In phone conversations, be aware of verbal and non-verbal clues
- Talk to the patient with reassurance and confidence



AVOID

- Making assumptions on the patient's level of knowledge and understanding
- Disregarding the carer
- Forgetting to actively listen
- Having one-way conversations with patients
- Relying only on verbal information in phone conversations



STEP 3

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INFORM AND EDUCATE

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LEARNING OBJECTIVE

INFORM AND EDUCATE

WHAT

WILL YOU LEARN?

In this section you will learn all about **informing and educating** the patient, addressing their knowledge gaps

WHY

IS THIS IMPORTANT?

An appropriate level of knowledge on the side of the nurse is essential for educating the patient

Informing and educating the patient in the right way is critical in **managing their treatment successfully**

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THE RIGHT KNOWLEDGE

- As a nurse is it essential to have up-to-date **knowledge** on:
 1. The **disease** and common symptoms
 2. The **diagnostic studies** that can be performed, the indications, methods and potential outcomes
 3. The **treatment aims and options**
 4. Potential **side effects and proactive management**
- Be aware of the type of information that is relevant for each individual patient, considering the patient's knowledge level and preferences

THE RIGHT KNOWLEDGE

DISEASE, SYMPTOMS AND DIAGNOSTICS

Examples of resources for healthcare professionals



Examples of resources for patients



- It is important to have a **detailed understanding of the pathophysiology, symptoms and diagnostic studies** related to metastatic CRC
- There are many **high-quality information sources** available to help you gather this background knowledge, as well as to refer patients to

Click on the image links above to visit the relevant website.

THE RIGHT KNOWLEDGE

TREATMENT AIMS AND OPTIONS

Treatment goals for advanced lines of treatment for metastatic CRC^{1,2}

Prolongation of survival

Alleviation of tumour-related symptoms

Maintaining quality of life (QoL)
Role functioning
Activities in daily life

Disease control
Prolonged stable disease / progression-free survival (PFS)

Balancing potential benefits against likely treatment toxicity

Respecting patient preference in decision making



Be aware that the patient's goals and preferences may change over time, as symptoms increase, side effects mount or QoL declines

THE RIGHT KNOWLEDGE

TREATMENT AIMS AND OPTIONS

Treatment options in third-line treatment of metastatic CRC, according to ESMO and NCCN guidelines¹⁻³

The treatment choice is dependent on patient and disease factors, including the mutation status of the tumor and the patient's performance status and treatment history.

Patients with *RAS* or *BRAF* wild-type disease not previously treated with EGFR antibodies

- ESMO¹
 - Cetuximab
 - Panitumumab
- NCCN^{2,3}
 - Cetuximab
 - Panitumumab
 - Cetuximab/panitumumab + irinotecan
 - Cetuximab/panitumumab + FOLFIRI

Patients pre-treated with fluoropyrimidines, oxaliplatin, irinotecan, bevacizumab and, if *RAS* wild-type, with EGFR antibodies

- Regorafenib¹⁻³
- Trifluridine + tipiracil (TAS-102)¹⁻³

THE RIGHT KNOWLEDGE

MOA OF REGORAFENIB & TAS-102



REGORAFENIB

- Orally administered therapy that inhibits protein kinases associated with angiogenesis (i.e. VEGFR1, VEGFR2, VEGFR3, TIE2), oncogenesis (i.e. KIT, RET, RAF1, BRAF), the tumour microenvironment (i.e. PDGFR, FGFR), and tumour immunity (CSF1R)¹⁻⁵
- Administered QD for the first 21 days of each 28-day cycle³
- Recommended in mCRC patients previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF therapy, and if RAS wild-type, an anti-EGFR therapy³

TRIFLURIDINE + TIPIRACIL (TAS-102)

- Orally administered combination of trifluridine (an antineoplastic thymidine-based nucleoside analogue) and a thymidine phosphorylase inhibitor that prevents degradation of trifluridine and has anti-neoplastic properties^{2,6}
- Administered twice daily within 1 hour of completing the morning and evening meals on days 1–5 and 8–12 of each 28-day cycle⁷
- Recommended in mCRC patients previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy⁷

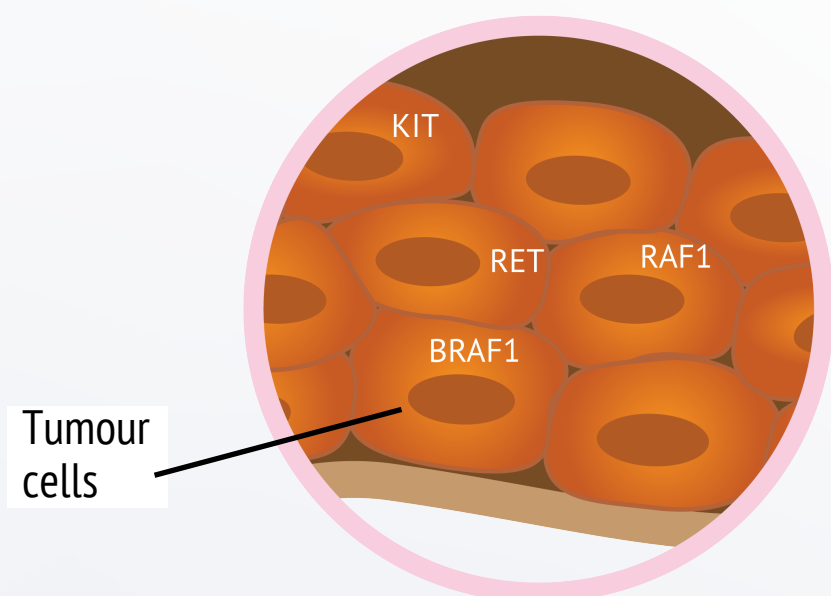
THE RIGHT KNOWLEDGE

MOA OF REGORAFENIB

Step 1

Oncogenesis

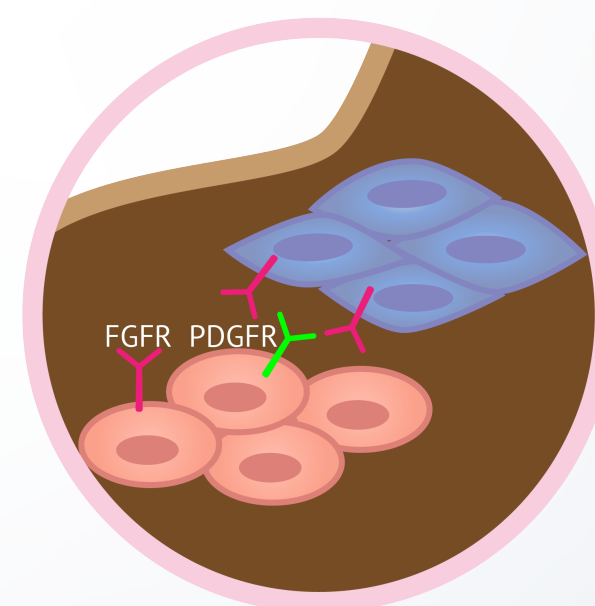
regorafenib inhibits multiple protein kinases in tumour cells, including KIT, RET, RAF-1 and BRAF-1, which are important oncogenesis.



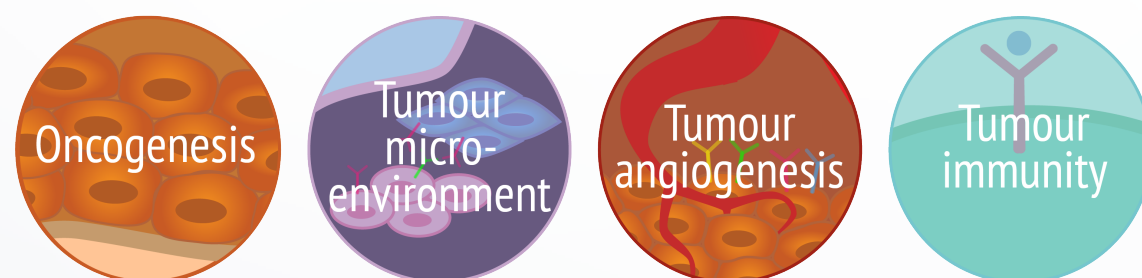
Step 2

Tumour microenvironment

regorafenib inhibits the protein kinases FGFR and PDGFR involved in regulation of the tumour microenvironment



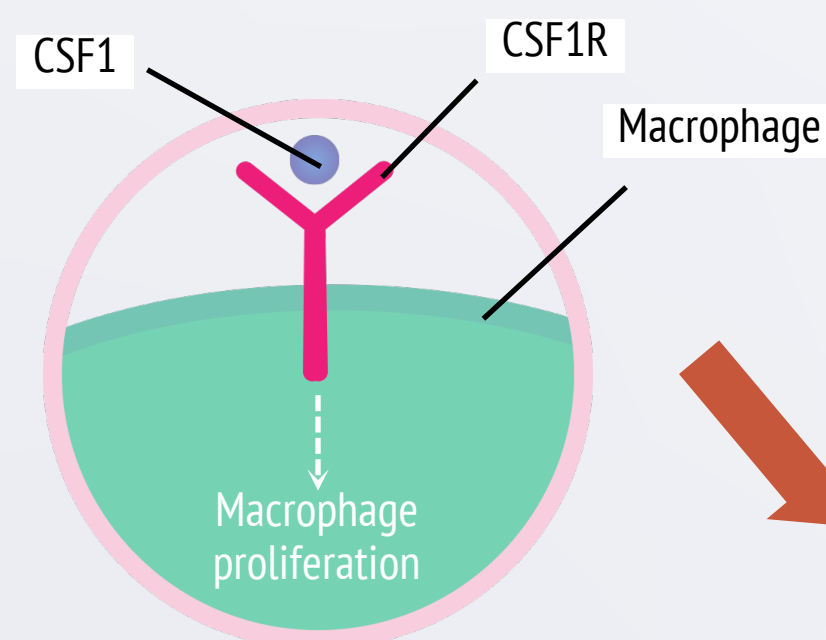
regorafenib targets normal cellular functions and pathological processes:



Step 4

Tumour immunity

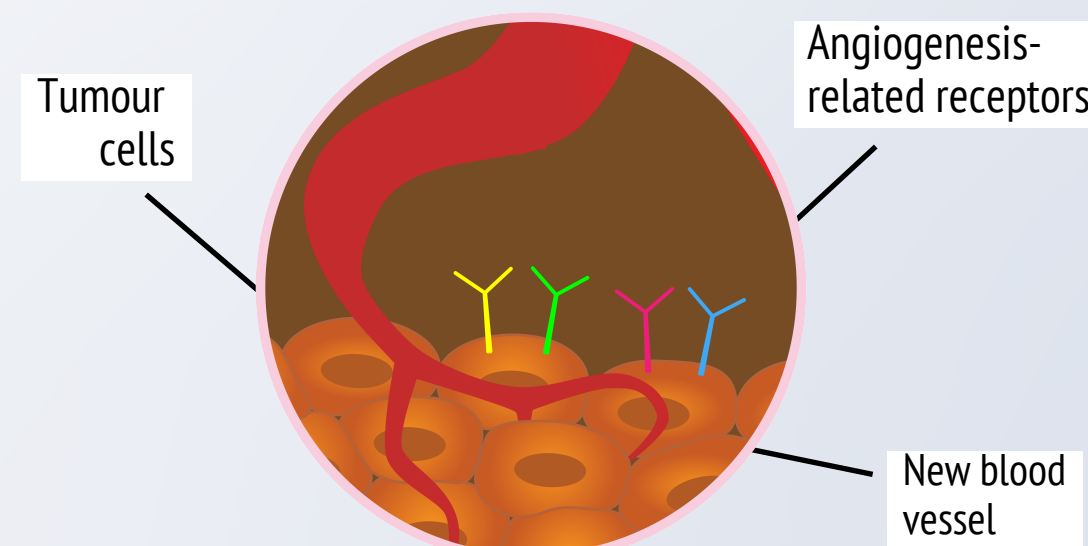
regorafenib inhibits CSF1R a receptor involved in macrophage proliferation, thereby disrupting tumour immunity.



Step 3

Tumour angiogenesis

regorafenib inhibits the protein kinases VEGFR 1 to 3 and TIE2 involved in tumour angiogenesis.



All four of these mechanisms contribute to the anti-cancer effects of regorafenib.



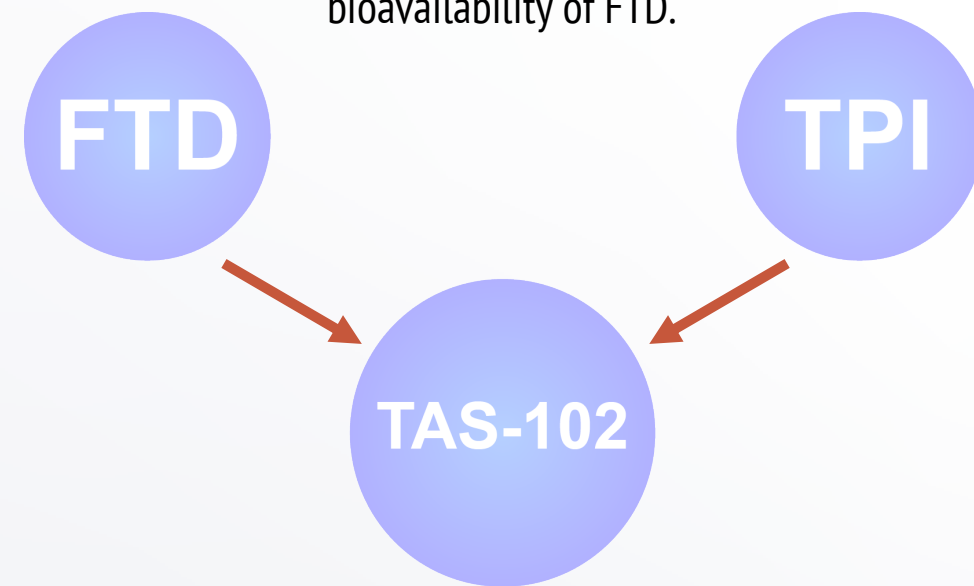
BRAF-1, B-Raf proto-oncogene, serine/threonine kinase; CSF1, colony stimulating factor 1; CSF1-R, colony stimulating factor 1 receptor; FGFR, fibroblast growth factor receptor, KIT, KIT proto-oncogene receptor tyrosine kinase; MOA, mechanism of action; PDGFR, platelet-derived growth factor receptor; RAF-1, Raf-1 proto-oncogene, serine/threonine kinase; RET, ret proto-oncogene; TIE2, angiopoietin-1 receptor; VEGFR, vascular endothelial growth factor receptor.

THE RIGHT KNOWLEDGE

MOA OF TAS-102

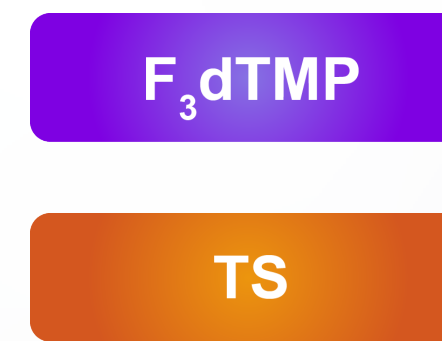
Step 1

TAS-102 is an oral combination drug consisting of trifluridine (FTD), a thymidine analog, and a TP inhibitor (TPI; tiparacil hydrochloride). TPI prevents rapid metabolism of FTD, thereby increasing the bioavailability of FTD.



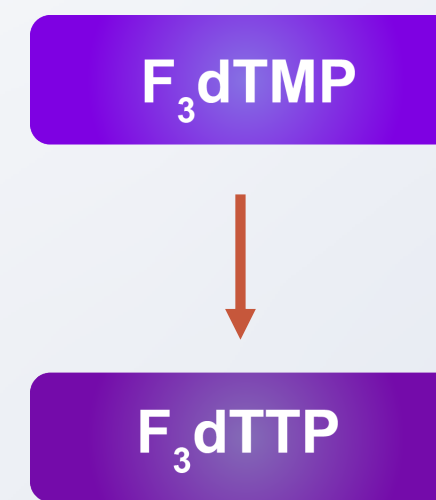
Step 2

FTD is phosphorylated by thymidine kinase (TK) and converted to the active molecule F_3dTMP . This binds to thymidylate synthase (TS) and blocks the thymidine formation required for DNA synthesis.



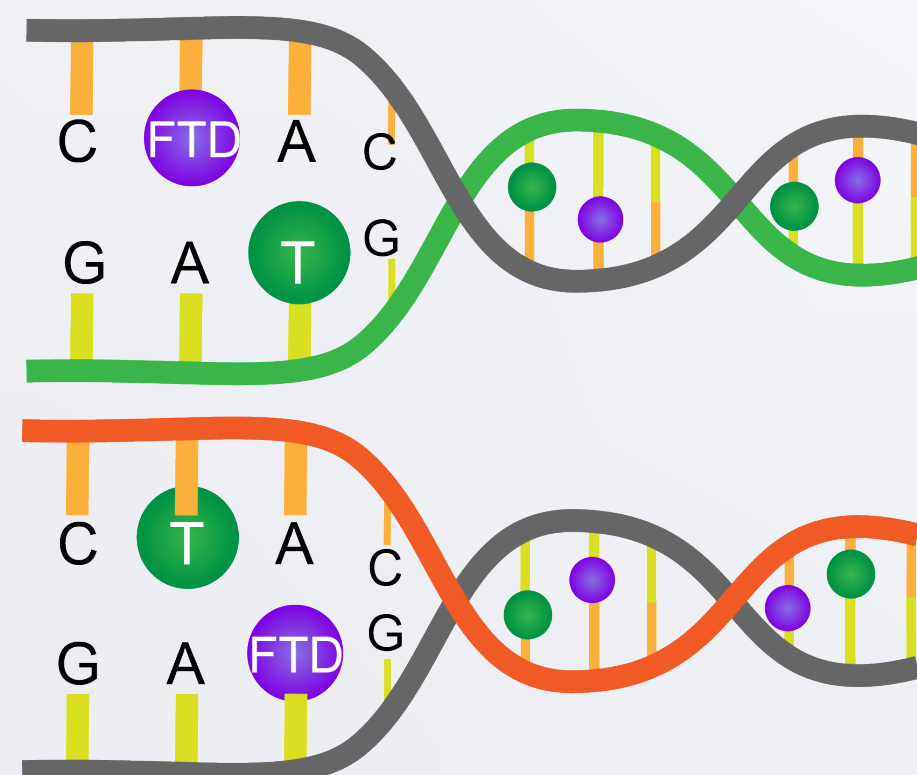
Step 3

Subsequent phosphorylations produce F_3dTTP , which is directly incorporated into the DNA, and induces DNA strand breaks.



Step 4

Although phosphorylated FTD does inhibit TS, this activity is secondary to its direct effects on DNA when administered orally.



F3dTDP, trifluorodeoxythymidine diphosphate; F3dTMP, trifluorodeoxythymidine monophosphate; F3dTTP trifluorodeoxythymidine triphosphate; FTD, trifluridine; MOA, mechanism of action; T, thymidine

THE RIGHT KNOWLEDGE

TREATMENT AIMS AND OPTIONS

- **Regorafenib and TAS-102** have shown **significant clinical benefits** in terms of overall survival (OS, primary endpoint), PFS and disease control as third-line treatments for metastatic CRC in phase 3 clinical trials versus placebo¹⁻⁴
 - However, the improvement in duration of OS from third-line treatments for metastatic CRC is generally modest
- There are limited **directly comparative data** of third-line therapies
- The **treatment choice** should depend on
 - Patient characteristics
 - Disease characteristics
 - Treatment goals
 - Treatment history

THE RIGHT KNOWLEDGE

EFFICACY: REGORAFENIB



Regorafenib phase 3 trial efficacy outcomes

	CORRECT ¹			CONCUR ²		
	Regorafenib	Placebo	HR (p-value)	Regorafenib	Placebo	HR (p-value)
Median OS, months	6.4	5.0	0.77 (p=0.0052)	8.8	6.3	0.55 (p=0.00016)
Median PFS, months	1.9	1.7	0.49 (p<0.0001)	3.2	1.7	0.31 (p<0.0001)
Median time to progression (TTP)	Not reported			Not reported		
Overall response rate (ORR), %	1.0	0.4	p=0.19	4	0	p=0.045
Disease-control rate (DCR), %	41	15	p<0.0001	51	7	p<0.0001

Pink cells: statistically significant effect shown

HR, hazard ratio; OS, overall survival; PFS, progression-free survival

1. Grothey A, et al. Lancet. 2013;381:303-12. 2. Li J, et al. Lancet Oncol. 2015;16:619-29.

THE RIGHT KNOWLEDGE

EFFICACY: TAS-102



TAS-102 phase 3 trial efficacy outcomes

	RECOURSE ¹			TERRA ²		
	TAS-102	Placebo	HR (p-value)	TAS-102	Placebo	HR (p-value)
Median OS, months	7.1	5.3	0.68 (p<0.001)	7.8	7.1	0.79 (p=0.035)
Median PFS, months	2.0	1.7	0.48 (p<0.001)	2.0	1.8	p<0.001
Median time to progression (TTP)	Not reported			Not reported		
Overall response rate (ORR), %	1.6	0.4	p=0.29	1.1	0	p=0.554
Disease-control rate (DCR), %	44	16	p<0.001	44.1	14.6	p<0.001

Pink cells: statistically significant effect shown

HR, hazard ratio; OS, overall survival; PFS, progression-free survival

1. Mayer RJ, et al. N Engl J Med. 2015;372:1909-19. 2. Xu J, et al. J Clin Oncol. 2018;36:350-58.

THE RIGHT KNOWLEDGE

REGORAFENIB FLEXIBLE DOSING

The ReDOS and REARRANGE trials have evaluated a flexible dosing strategy with regorafenib in the first treatment cycle¹⁻²
The NCCN guidelines recommend dose escalation as an appropriate alternative approach for regorafenib dosing³

ReDOS¹

- Randomised, open-label, **phase 2** trial in 123 patients with refractory metastatic CRC, comparing:
 - Standard-dose regorafenib: 160 mg/day for 3 weeks on/1 week off
 - Dose escalation: 80 mg/day in week 1, 120 mg/day in week 2 and 160 mg/day in week 3, provided no significant drug-related AEs occurred
- Results
 - In the **dose-escalation group, significantly more patients initiated cycle 3** vs the standard-dose group (43% vs 26%; P=0.043)
 - Dose escalation did not seem to jeopardize efficacy
 - **AEs were similar** between the two groups
 - The severity of some toxicities, including HFSR, might be slightly lower in the dose-escalation group

REARRANGE²

- Randomised **phase 2** trial in 299 patients with metastatic CRC, comparing:
 - Standard dose (160 mg/day 3 weeks on/1 week off)
 - Reduced dose (120 mg/day 3 weeks on/1 week off)
 - Intermittent dosing (160 mg/day 1 week on/1 week off)
- Results
 - There was **no difference in survival outcomes** and the trial did **not meet its primary endpoint of improving global tolerability** in the reduced and intermittent dose groups
 - Flexible dosing showed a **numerical improvement in relevant AEs**, including fatigue, HFSR and hypertension

THE RIGHT KNOWLEDGE

PROACTIVE MANAGEMENT OF SIDE EFFECTS

Most common AEs*

Regorafenib¹

- Asthenia/fatigue
- Pain
- Decreased appetite and food intake
- HFSR
- Diarrhoea
- Mucositis
- Weight loss
- Infection
- Hypertension
- Dysphonia

TAS-102²

- Asthenia/fatigue
- Nausea
- Decreased appetite
- Diarrhoea
- Vomiting
- Abdominal pain
- Pyrexia
- Infections
- Haematotoxicity (anaemia, neutropenia, thrombocytopenia)

Effective AE management requires:

- **Awareness** of the patient's medical and treatment history
- **Close communication** between the patient, carers and healthcare professionals³
- **Early identification and management** of AEs can prevent them from worsening
- Many AEs can be effectively managed with supportive measures and/or medication as well as treatment modification⁴
- Preventative measures
- Clear grading guidelines

*The most common AEs, as reported in the prescribing information, occurring in $\geq 30\%$ and $\geq 10\%$ of patients in clinical trials with regorafenib (CORRECT study) and TAS-102 (RECOURSE study), respectively.

AE, adverse event; HFSR, hand-foot skin reaction

1. Stivara (regorafenib) Prescribing Information 2019. 2. Lonsurf (TAS-102) Prescribing Information 2019. 3. Grothey A, et al. *Oncologist*. 2014;19:669-80. 4. Rogers, JE. *Onco Targets Ther*. 2017;10:2033-44.

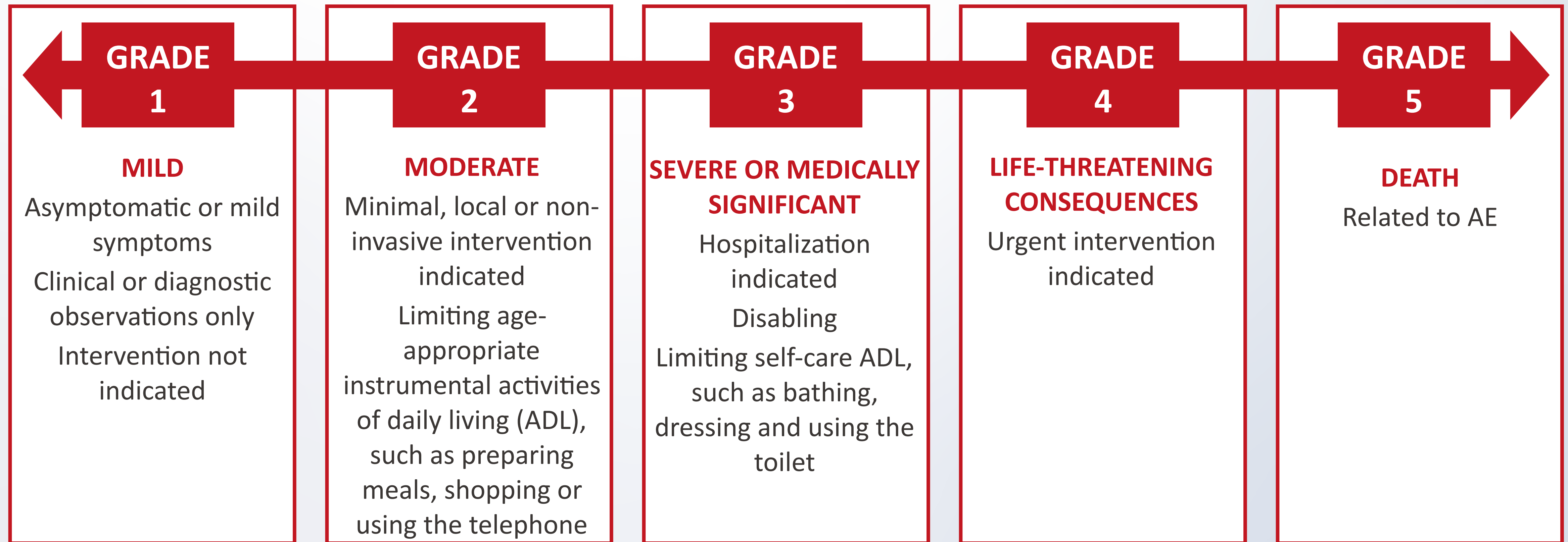
THE RIGHT KNOWLEDGE

GRADING SIDE EFFECTS

VISIT CTAE VERSION 5.0 WEBSITE



- Effective AE management requires **clear grading guidelines**
- Universal grading of AEs **allows for universal management of AEs**, including dose modifications
- The Common Terminology Criteria for Adverse Events (**CTCAE**) is often used for grading AEs. Version 5.0 of the CTCAE can be accessed above



THE RIGHT KNOWLEDGE

PROACTIVE MANAGEMENT OF SIDE EFFECTS OF REGORAFENIB

AE	Symptoms	Onset	Resolution	Prevention and general management
HFSR	<ul style="list-style-type: none"> •Numbness, tingling, pins and needles on hands and feet •Abnormal or increased sensitivity to touch •Pain or burning sensation •Calluses •Scaly, dry, cracked, peeling or flaking skin 	2-4 weeks after starting therapy		<ul style="list-style-type: none"> •Control calluses •Comfort and cushion •Cover with creams •Sunscreen use; limit sun exposure •Avoid irritants •Wear comfortable clothing
Rash/desquamation	<ul style="list-style-type: none"> •Redness •Itchiness •Dry, peeling, flaking skin •Flat, discoloured skin •Blistering •Can appear anywhere on the body; most common on the face, forehead, scalp, upper chest and back 	Most common in the first few weeks after starting therapy	Early detection and management typically leads to full resolution	<ul style="list-style-type: none"> •Careful choice of skincare products •Sunscreen use; limit sun exposure •Caution around heat
Fatigue	<ul style="list-style-type: none"> •Tired eyes or legs •Stiff shoulders •Whole body tiredness •Sleepiness •Lack of energy •Boredom; no motivation 	Typically within first month of treatment	Early reporting and management facilitate resolution	<ul style="list-style-type: none"> •Some causes are treatable •Set priorities •Rest and recharge
Diarrhoea	<ul style="list-style-type: none"> •≥ 3 loose stools per day or more frequent bowel movements beyond what is normal for the patient 			<ul style="list-style-type: none"> •Should be promptly managed to avoid dehydration •Prescribed anti-diarrhoeal treatments •Hydration •Eating frequent, small meals •Being aware of triggers
Oral mucositis	<ul style="list-style-type: none"> •Sores in the mouth, gums, or tongue •Swelling or soreness in the mouth without sores •Pain or burning sensation in the mouth •Altered or distorted sense of taste •Difficulty or discomfort eating or swallowing 	Typically within 14 days of starting treatment		<ul style="list-style-type: none"> •Prescription treatments •Practice of good oral care •Hydration •Eating soothing foods

AE, adverse event; HFSR, hand-foot skin reaction

Bayer Pharma AG. ARGO study patient information: tips for managing common side effects. 2016.

THE RIGHT KNOWLEDGE

PROACTIVE MANAGEMENT OF SIDE EFFECTS OF TAS-102

AE	Onset	Resolution	Prevention and general management
Fatigue			<ul style="list-style-type: none"> • Sleep hygiene strategies (e.g. napping, exercise, avoiding overexertion, bedtime routine)
Nausea	< 7 days of starting treatment		<ul style="list-style-type: none"> • Consuming small meals or warm/cool foods or beverages • Avoiding irritating foods (e.g. greasy, fried, sweet, spicy) • Using antiemetics
Vomiting	35 (12–36) days*		<ul style="list-style-type: none"> • Consuming small meals or warm/cool foods and beverages • Avoiding irritating foods (e.g. greasy, fried, sweet, spicy) • Using antiemetics • Drinking liquids to avoid dehydration
Decreased appetite			<ul style="list-style-type: none"> • Eating smaller meals • Avoiding solid foods (drinking/eating i.e. milkshakes, smoothies, juice, soup) • Choosing foods high in calories or protein • Increasing physical activity to stimulate hunger
Diarrhoea	38 (14–74) days* At any time in 1 st cycle	Tends to resolve quickly	<ul style="list-style-type: none"> • Eating smaller meals, low-fibre foods • Eat foods high in sodium and potassium (i.e. bananas, oranges, peaches, apricots, potatoes) • Drinking liquids at room temperature slowly
Abdominal pain			<ul style="list-style-type: none"> • Avoiding foods that produce gas • Eating fibre-rich foods • Regular exercise
Pyrexia			<ul style="list-style-type: none"> • Drinking liquids to avoid dehydration • Rest • Keeping cool
Interstitial lung disease	Median time: 51 days (range 22–91)	Median duration: 10 days (range 7–39)	<ul style="list-style-type: none"> • Early diagnosis • Monitoring • Medical management (e.g. antibiotic or corticosteroid therapy, bronchoalveolar lavage)
Anorexia	< 7 days of starting treatment		<ul style="list-style-type: none"> • Eating smaller meals • Avoiding solid foods (drinking/eating i.e. milkshakes, smoothies, juice, soup) • Choosing foods high in calories or protein

*Median (range) time to nadir for grade ≥ 3 AEs.

AE, adverse event

1. Van Cutsem E, et al. ASCO GI 2017. Abstract #788. 2. Yoshino T, et al. Clin Colorectal Cancer. 2016;15:e205-e11. 3. Lonsurf (trifluridine and tipiracil) tablets. (Accessed November 11, 2019 at www.lonsurf.com) 4. European Medicines Agency. Lonsurf Assessment Report (EMA/H/C/003897/0000). 2016. 5. Kamei Hetal. J Med Case Rep. 2016;10:310. 6. Jeffers KD. J Adv Pract Oncol. 2016;7:449-53.

THE RIGHT KNOWLEDGE

MANAGEMENT OF SIDE EFFECTS



For **more information** on the proactive management of side effects, please refer to these publications and guideline.

VISIT ESMO ONCOLOGY PRO



Information on the management of skin toxicity, for healthcare professional and patients

VISIT MASCC MUCOSITIS GUIDELINES



Information on the management of oral mucositis

VISIT MASCC ANTIEMETICS GUIDELINES



Information on the management of nausea and vomiting

VISIT KRISHNAMOORTHY et al



Review paper on the management of regorafenib-related toxicities

VISIT SASTRE et al



Review paper on the clinical management of regorafenib

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WHAT NEEDS TO BE EXPLAINED TO THE PATIENT

FILL THE **GAPS IN THE PATIENT'S KNOWLEDGE**

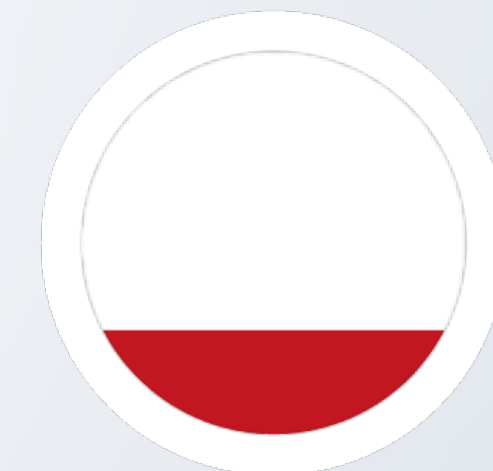
For more information on the **Ask, Tell, Ask** model, please refer to:

- The paper "If We Don't Ask, Our Patients Might Never tell: The Impact of the Routine Use of a Patients Values Assessment" by J. Russell Hoverman et al.

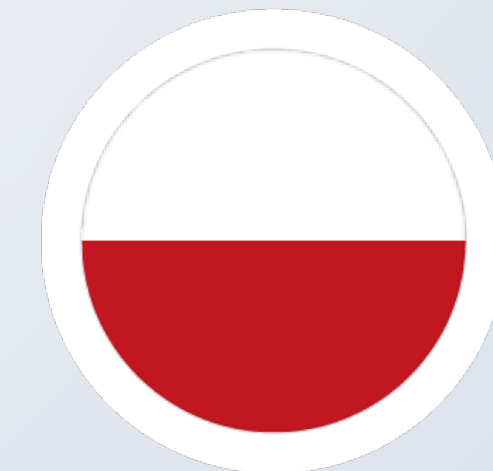
[DOWNLOAD THE PAPER](#) 

- This video by research nurse Connie Davis, by the Institute for Healthcare Improvement

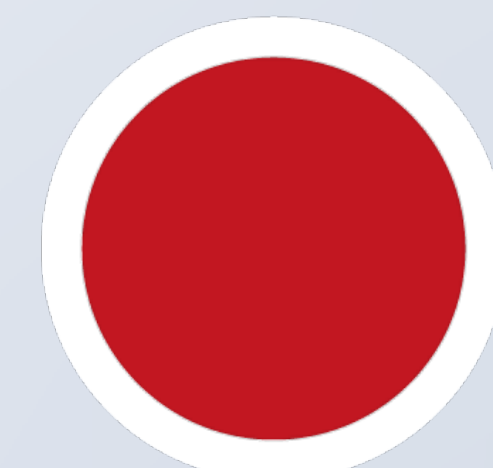
[VIEW THE VIDEO](#) 



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THE RIGHT WAY TO DELIVER THE MESSAGES

- Continue to use the **Ask, Tell, Ask model** to discover knowledge gaps and efficiently educate patients
- Acknowledge the patient's **emotions**
- Ask if they **wish and are ready to hear and understand** more information before you continue
- **Repeat** information as often as needed
- Listen actively
- Continue to involve the carer
- Use patient-friendly language
- Use **printed and/or written materials** to embed knowledge



Practical tips:

- When printed materials are not available, consider simply **writing** a brief summary or **drawing** a quick diagram supporting your explanation for patients to take with them.
- Remember to educate the patient with **reassurance and confidence**.

STEP 3

SUMMARY

INFORM AND EDUCATE

DO

- Make sure you are up to date with the latest information and are comfortable explaining the disease and common symptoms, diagnostic studies, treatment aims and options and proactive management of AEs
- Use the Ask, Tell, Ask model to efficiently educate patients and fill in the gaps in their knowledge
- Allow patients the opportunity to ask questions
- Use patient-friendly language
- Talk to the patient with reassurance and confidence



AVOID

- Letting your own level of knowledge slide, so you no longer feel confident in front of patients
- Making assumptions on the patient's level of knowledge and understanding
- Ignoring questions from the patient, even if you cannot answer them at that time
- Having one-way conversations with patients



STEP 4

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DIRECT TO ADDITIONAL SUPPORT

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LEARNING OBJECTIVE

DIRECT TO ADDITIONAL SUPPORT

WHAT WILL YOU LEARN?

In this section you will learn all about directing the patient and the carer to **additional support**

WHY IS THIS IMPORTANT?

Navigating patients towards help addressing their full **spectrum of needs** is an important part of a successful treatment journey

THE RIGHT KNOWLEDGE

A SPECTRUM OF EXPERTISE

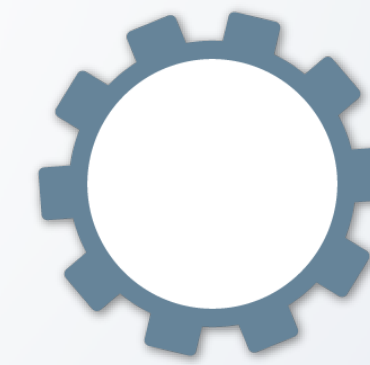
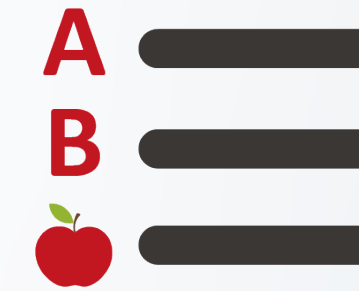
- It is important to **be aware of the local options** for additional support in your centre and region
- Know how to **deal with sensitive issues**, such as emotional, spiritual, social and financial issues
- Remember the need for **supporting the carer** as well as the patient

Patient associations, such as Fight Colorectal Cancer, the Colorectal Cancer Alliance and Digestive Cancers Europe, can also provide support for patients and families.



WHAT NEEDS TO BE EXPLAINED TO THE PATIENT

- What **options** the patient has beyond the drugs
 - Including the importance of maintaining a **healthy lifestyle**
- How the patient can access this support, helping patients to **navigate the healthcare system**
- That you can **guide** patients in dealing with **other issues**, such as social or financial issues
 - The patient is not alone: there is a network of people to help the patient and the carer
- Make sure the patient is aware of the support options available, even if they are **not directly relevant** at this time
- Be aware of emotional fatigue on the part of **carers**, so you can direct them to additional support
 - There are specific support services for carers, including respite programs and social-worker sessions for family members



CARER'S GUIDE

 DIGESTIVE CANCERS
EUROPE

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WHAT NEEDS TO BE EXPLAINED TO THE PATIENT

ADVANCED CARE PLANNING



- The following **topics** can be addressed when discussing advanced care planning¹:
 - **Prognosis**, sharing it as a range, tailored to information preferences
 - The patient's most important **goals** if the health situation worsens
 - The patient's biggest health-related **fears and worries**
 - The **abilities** so critical that patients cannot imagine **living without them**
 - The awareness of the **family** about the patient's priorities and wishes
 - For more information, please refer to the [Serious Illness Conversation Guide](#)

- Advanced care planning includes discussing practical matters:
- Completing a **living will**, including the patient's wishes related to life-sustaining treatment (e.g. MOLST or POLST forms)
- Signing a **do not resuscitate order**
- Naming a **healthcare proxy**, a person who can make healthcare decisions for the patient when he/she becomes unable to make or communicate those decisions
- Naming a **principal**, who is given durable power of attorney to act on the patient's behalf in a broad range of matters, such as buying and selling real estate and managing finances

THE RIGHT WAY TO DELIVER THE MESSAGES

- As a nurse, it is important to sense **emotional and psychological changes** in your patient, such as anxiety or signs of depression
- If patients have issues you cannot resolve immediately, this does not mean you cannot help, as you help by **putting the patient in touch with the correct experts**

Practical tips:

- If patients say “no” to a support option, encourage them to reconsider
- For example: some patients may say “no” as they find it difficult to admit they need mental-health support or fear they are not fit enough to participate in a training programme
- It can be helpful for patients to hear the nurse’s opinion regarding whether they think it is a good idea
- Some patients will feel reassured by making them feel you have guided a lot of patients like them – inspiring them to know that they are not the first to enter upon this journey
- Be aware of the caveat that you do not want this to make patients feel they have become a ‘number’
- Communicate with reassurance and confidence

THE RIGHT WAY TO DELIVER THE MESSAGES

OTHER TREATMENT OPTIONS

- Be **open to other options** the patient feels may be beneficial
 - Open communication allows you to ensure the patient is sensible about trying other options
- When a patient wants to try other options, such as supplements or herbal medicines, be **mindful of interactions** with prescription medication
- **Appreciate the psychological support** that patients may feel they gain from more holistic therapies versus conventional medicine, despite the lack of scientific evidence
- Take a **supportive position**, within the realm of safety

Practical tips:

- Ask patients to bring a list of the exact preparations they are thinking of using, review it with the pharmacist and then counsel the patient on possible interactions and risks of decreased efficacy or increased side effects.

STEP 4

SUMMARY

DIRECT TO ADDITIONAL SUPPORT

DO

- Have open conversations with patients about the support they need beyond the drugs, for physical, mental, emotional, spiritual, social, financial or work-related issues
- Act as a guide for your patients to navigate through the healthcare system
- When applicable, advanced care planning should also be part of this conversation
- Consider the carers and encourage them to have an active role
- Talk to the patient with reassurance and confidence



AVOID

- Being unaware of the local support options beyond the drugs
- Focusing solely on the oncologic treatment
- Regarding the patient's non-medical issues to be outside of your scope
- Closing the door on conversations about unconventional treatment options, such as herbal medications
- Disregarding the carer



STEP 5

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EMPOWER THE PATIENT

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LEARNING OBJECTIVE

EMPOWER THE PATIENT

WHAT

WILL YOU LEARN?

In this section you will learn all about **empowering the patient**, making patients feel they can actively participate in the shared decision-making and treatment process, with the medical team there for them every step of their way

WHY

IS THIS IMPORTANT?


Patient empowerment increases the likelihood of treatment success

THE RIGHT KNOWLEDGE

REINFORCING THE KNOWLEDGE CIRCLE

- **Be fully aware of the individualised treatment and care plan** for every patient, including:
 - Next steps
 - When patients should contact the hospital
 - Who they should contact and how
- A **positive, hopeful approach** gives patients strength and confidence throughout their treatment journey
 - It is important to let patients know they are **doing everything right**. Any positivity (e.g. your labs look good, you are doing great so far) **boosts the patient's morale**
- Accept that some information will need to be **continually repeated**
 - Such as the need for treatment compliance and information on side effects
- **Feed back** the information you gathered on the patient **to the MDT**
 - For example: signs of depression, increased pain or a need for a consultation by a dermatologist or physiotherapist

WHAT NEEDS TO BE EXPLAINED TO THE PATIENT



WHAT THE
PATIENT CAN
EXPECT NEXT

WHAT



WHEN TO
CONTACT THE
HOSPITAL

WHEN



WHO TO
CONTACT
AND HOW

WHO

- Emphasise that the **patient is in control** of his/her treatment journey
 - The multidisciplinary healthcare team will partner with them, but ultimately patients can make their own choices

THE RIGHT WAY TO DELIVER THE MESSAGES

- Recognise that **clarity** on the next steps **provides comfort** to patients
- Provide **hope and positive feedback**
 - Avoid giving false hope or unrealistic expectations
- Emphasise the **ongoing nature** of the nurse-patient relationship
- Include the **carer**
- Use **printed and/or written materials** to embed knowledge

Practical tips:

- Remember to communicate with **reassurance and confidence.**



STEP 5

SUMMARY

EMPOWER THE PATIENT

DO

- Take a positive, hopeful approach
- Accept that some information will need to be continually repeated
- Be clear on the next steps, providing comfort to patients
- Emphasise that the patient is in control
- Emphasise the ongoing nature of the nurse-patient relationship
- Involve the carer
- Use printed/written materials to embed knowledge



AVOID

- Neglecting patient empowerment
- Giving false hope or unrealistic expectations
- Forgetting to talk about the next steps, as this will lead to insecurity for your patient
- Forceful communication
- Focusing on the negatives



SUMMARY & CLOSE

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BEFORE YOU GO...

- **Thank you** for participating in this educational programme on the GUIDE communication framework
- You should now **feel more confident** to educate and empower patients treated for CRC and be able to respond to a fully comprehensive range of questions
- **You now know**
 - **how to explain** the aspects of CRC and its treatment that are essential for the patient to understand
 - **how to optimise your support** for patients, to enhance understanding and to drive adherence
 - **how to apply the GUIDE framework** across a variety of interactions, to strengthen shared decision-making and to deliver the best possible care
- We hope you have found this useful for your daily practice

BEFORE YOU GO...

- Throughout the e-learning and slide set, there are **links to additional information and resources**. If you wish, you can always revisit either resource at any time and dig deeper into a specific topic
- At www.nursesconnect.info you will find the full video on the GUIDE framework, as well as many other initiatives from the GI NURSES CONNECT group
- Please proceed now to the **assessment quiz to test your knowledge**
- Completing this educational programme may be recognised by the CME accreditation system in your country. After passing the assessment quiz, you can print your certificate on the course home page on Checkpoint

SUMMARY

The **GUIDE** communication framework

WHAT

THE **GUIDE** COMMUNICATION FRAMEWORK

- Is a 5-step communication framework to improve the benefit of nurse-patient interactions
- Supports nurses in their role as a knowledgeable go-to person for patients with CRC, strengthening shared decision-making and delivering the best possible care
- Includes a memory aid – **GUIDE**
- May be delivered over several interactions and should be adapted depending on patient needs

WHY

IS THE COMMUNICATION FRAMEWORK NEEDED

- Nurses are to be regarded as a go-to person for their patients with CRC and therefore must
 - empower patients through guidance and support throughout the treatment journey
 - be an active member of the MDT in delivering shared decision-making
- so they can provide patients with the greatest chance of success

GUIDE

GUIDE's five letters each represent a crucial step in your conversations with patients with CRC.

Gain insight into the goals of treatment and care

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Understand the gaps in the patient's knowledge

U

Inform and Educate

I

Direct to additional support

D

Empower the patient

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THE GUIDE COMMUNICATION FRAMEWORK IS SUPPORTED BY FIGHT COLORECTAL CANCER



- The importance of supportive and open nurse-patient conversations is acknowledged by patient advocacy groups
- This e-learning was supported by Fight CRC. They fight to cure colorectal cancer and serve as relentless champions of hope for all affected by this disease through informed patient support, impactful policy change, and breakthrough research endeavours
- For more information, including a library of resources for patients (<https://fightcolorectalcancer.org/resources/>), visit the Fight CRC website: www.fightcolorectalcancer.org

COR2ED CHECKPOINT

COR2ED Checkpoint, made available on <https://checkpoint.cor2ed.com> and organised by COR2ED, is accredited by the European Accreditation Council for Continuing Medical Education (EACCME) to provide the following CME activity for medical specialists.

Each medical specialist should claim only those credits that he/she actually spent in the educational activity. The EACCME is an institution of the European Union of Medical Specialists (UEMS). Only those e-learning materials that are displayed on the UEMS-EACCME website have formally been accredited.

Through an agreement between the European Union of Medical Specialists (UEMS) and the American Medical Association (AMA), physicians may convert EACCME credits to an equivalent number of AMA PRA Category 1 Credits™.

Information on the process to convert EACCME credit to AMA credit can be found at www.ama-assn.org/education/earn-credit-participation-international-activities



ACKNOWLEDGMENT, DISCLAIMER & DISCLOSURES

- The full programme is supported by an Independent Educational Grant from Bayer
- The material and content contained within this slide deck are for healthcare professionals only
- The material is provided for informational and educational purposes only. The information provided is not intended as a substitute for medical professional help, advice, diagnosis or treatment and may not be applicable to every case or country
- The views of the GI NURSES CONNECT members responsible for creating this resource are their own personal opinion. They do not necessarily represent the views of the members' academic or medical institutions or the rest of the GI NURSES CONNECT group
- Fransen McGinley, Nina Grenon and Sven De Keersmaecker do not have any relevant financial relationships to disclose.

ABBREVIATIONS

- **AE**, adverse event
- **AGCNP-BC**, Adult-Gerontology Primary Care Nurse Practitioner Certification
- **AOCN**, Advanced Oncology Certified Nurse
- **BRAF-1**, B-Raf proto-oncogene, serine/threonine kinase
- CRC, colorectal cancer
- **CSF1R**, colony stimulating factor 1 receptor
- **CTCAE**, Common Terminology Criteria for Adverse Events
- **DCR**, disease control rate
- **DNP**, Doctor of Nursing Practice
- **EGFR**, epidermal growth factor receptor
- **ESMO**, European Society of Medical Oncology
- **FGFR**, fibroblast growth factor receptor
- **FOLFIRI**, folinic acid, fluorouracil, irinotecan
- **FOLFOX**, folinic acid, fluorouracil, oxaliplatin
- **GI**, gastrointestinal
- **GUIDE**, a communication framework that will help you have even better conversations with your patients, to educate and guide them throughout their cancer treatment journey. GUIDE's five letters each represent a crucial step in your conversations with patients with CRC
- **HFSR**, hand-foot skin reaction
- **HR**, hazard ratio
- **KIT**, KIT proto-oncogene receptor tyrosine kinase
- **MDT**, multidisciplinary team
- **MHS**, Master of Health Science
- **MOLST**, Medical Orders for Life-Sustaining Treatment
- **NCCN**, National Comprehensive Cancer Network
- **ORR**, overall response rate
- **OS**, overall survival
- **PA-C**, Certified Physician Assistant
- **PDGFR**, platelet-derived growth factor receptor
- **PFS**, progression-free survival
- **POLST**, Provider Orders for Life-Sustaining Treatment
- **QoL**, quality of life
- **RAF1**, Raf-1 proto-oncogene, serine/threonine kinase
- **RET**, ret proto-oncogene
- **RN**, Research Nurse
- **TIE2**, tyrosine kinase with immunoglobulin-like and EGF-like domains 2
- **TTP**, time to progression
- **VEGFR**, vascular endothelial growth factor receptor

REFERENCES

- Argilés G, et al. *Ann Oncol*. 2019;30(Suppl_4):O-026.
- Bekaii-Saab TS, et al. *Lancet Oncol*. 2019;20:1070-1082.
- Bernacki R, et al. *BMJ Open* 2015;5:e009032.
- Ellis LM, et al. *J Clin Oncol*. 2014;32:1277-80.
- European Medicines Agency. Lonsurf Assessment Report (EMA/H/C/003897/0000). 2016.
- Grothey A, et al. *Clin Adv Hematol Oncol*. 2016;14:1-15.
- Grothey A, et al. *Lancet*. 2013;381:303-12.
- Grothey A, et al. *Oncologist*. 2014;19:669-80.
- Hoverman JR, et al. *J Oncol Pract*. 2017;13:e831-e837.
- How Oncology Nurses Provide Quality Care Through Telephone Triage. *ONS Voice*. Nov 6, 2018. <https://voice.ons.org/news-and-views/how-oncology-nurses-provide-quality-care-through-telephone-triage>. Accessed on Jul 16, 2019.
- Jeffers KD. *J Adv Pract Oncol*. 2016;7:449-53.
- Kamei Hetal. *J Med Case Rep*. 2016;10:310.
- Li J, et al. *Lancet Oncol*. 2015;16:619-29.
- Lonsurf (TAS-102) Prescribing Information 2019.
- Lonsurf (trifluridine and tipiracil) tablets. (Accessed November 11, 2019 at www.lonsurf.com)
- Mayer RJ, et al. *N Engl J Med*. 2015;372:1909-19.
- NCCN. Rectal Cancer. Version 3.2019. September 26, 2019.
- NCCN. Colon Cancer. Version 4.2019. November 85, 2019.
- Ohhara Y, et al. *World J Gastrointest Oncol*. 2016;8:642-55.
- Rogers, JE. *Onco Targets Ther*. 2017;10:2033-44.
- Stivarga (regorafenib) Prescribing Information 2019.
- Stivarga (regorafenib) SmPC 2018. 5. Matsushime H, et al. *Cell*. 1991;65:701-3.
- Stivarga (regorafenib) Prescribing Information 2019.
- Uboha N, Hochster HS. *Future Oncol*. 2016;12:153-63.
- U.S. Department of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE). Version 5.0. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf. Accessed August 19, 2019.
- Van Cutsem E, et al. *ASCO GI 2017*. Abstract #788.
- Vogel A, et al. *Cancer Treat Rev*. 2017;59:54-60.
- Van Cutsem E, et al. *Ann Oncol*. 2016;27:1386-422;
- Xu J et al. *J Clin Oncol*. 2018; 36:350-58.
- Yoshino T, et al. *Clin Colorectal Cancer*. 2016;15:e205-e11.