Role of the Immune response in early stage colorectal cancers: a new era in precision medicine

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Colorectal cancer - Key figures

- CRC 2nd most lethal cancer and 3rd most common cancer worldwide

- 2018 1.8 million cases worldwide

- 5 year survival is 65% and goes down to 12% for metastatic disease

- 25% present late despite widespread screening

- Early disease treated with surgery ± chemo depending on stage
Key challenge in the early colorectal cancers is to prevent the relapse. Prevent the metastatic relapse with an effective patient management since early stage.

Colorectal cancer progression

- **Localized stage**
- **Regional stage**
- **Distant stage**

Assess with staging system

Classify the cancer progression

Chance of survival

- 90%* 5 years survival rate
- 71%*
- 14%*

SEER database
The CRC’s therapeutic strategy is based on incomplete risk-assessment tool.

Gold standard: TNM Classification

- **T**: tumour extension
- **N**: regional lymph nodes
- **M**: distant metastasis

TNM stage does not accurately reflect survival for many patients.

Reality for Patients based on TNM staging only:
- many Over-treated
- and some
- Under-treated

A need for additional biomarker to OPTIMIZE adjuvant treatment decisions.
Tumor profiling improved the TNM system and cancer prognosis

Staging system has been improved by a better understanding of tumor profile
The protective value of immunity was initially proposed by Paul Ehrlich in 1909; however, it was impossible to access the validity of the prediction due to limited awareness of the immune system.

Host immune assets from hope to reality... Immunomodulatory roles of nutritional, lifestyle, and pharmacological factors including omega-3 PUFA, vitamin D, physical activity.
Latest discoveries of the immune system's involvement in cancer progression with the advent of immunotherapy.

Presence of T-cells in the tumor can influence at each step of cancer progression.

The latest discoveries on the role of immune microenvironment massively changed our cancer diagnosis and treatment approach.
More important than clinico-pathological feature, the survival is predetermined by pre-existing immunity.

- Tumor progression, invasion and recurrence are dependent on pre-existing immunity.
- Pre-existing immunity is determining the fate and survival of the patient.
Include immune response, completes and refines knowledge about the patient's cancer.
As a key parameter now, the immune response can be measured to assess digestive tumors

- WHO Blue book is the gold standard for the diagnosis of tumors with regular updates to keep up to date to innovations

- This international authoritative reference book considers now immune response as an essential and desirable diagnostic criteria for colorectal cancer by the WHO

- The tool is likely to complement the traditional staging system (cf. TNM-I claim)
Key characteristics for a good biomarker

✓ Clinically validated: studies conducted on a large cohort of patients with consistent and similar results

✓ Accurate: Superior to current technologies

✓ Repeatable: same result as many times as you do the test

✓ Stable: stable results for all settings

✓ Applicable and available: in the routine practice, for all facilities
Difference between a **prognostic** and **predictive** diagnostic test

**Patient journey**

- **PREDICTIVE** Biomarker
  - **Diagnosis**
  - **Treatment**
  - **Remission**
  - **Will the TREATMENT benefit ME?**

- **PROGNOSTIC** Biomarker
  - **Diagnosis**
  - **Remission**
  - **Will my tumor RECURRE?**
  - My recurrence risk can guide my doctor to take the tailored clinical decision, so that I have the best chance of survival

**DIGESTIVE CANCERS EUROPE**

**MASTERCLASS SERIES – 2020 VIRTUAL EXPERIENCE**
Now, the immune response can be assessed and computed in a systemic score New biomarker

Driven by clinical use

A reliable estimate of the risk of recurrence in colon cancer*

* The prognostic value of Immunoscore; in patients with cancer: A pooled analysis of 10,328 patients Xingxia Zhang, IJBM2020
This new immune biomarker was validated in large international study published in one of the most reputable peer reviewed journals.

Key characteristics filled:

- Clinically validated
- Accurate
- Repeatable
- Stable
- Applicable, available

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**International validation of the consensus Immunoscoring for the classification of colon cancer: a prognostic and accuracy study**

A large-scale international clinical study validates the prognostic value of Immunoscoring® in colon cancer

- An international consortium confirms the strong prognostic value of the Immunoscoring® assay in early stage colon cancer.
- Published in *The Lancet* on May 11, 2018, these results validate the reliability of Immunoscoring® Colon in identifying patients with a high risk of recurrence, independently of the TNM® staging system.

**Analytical validation of the Immunoscoring and its associated prognostic value in patients with colon cancer**

Florence Markot, Xiaoyi Chen, Arno Kirillovsky, Thomas Stammatis, Carine El Eissly, Lucienna Batista, Marc Van den Eynde, Naïla Hachter-Adouni, Maria-Gabriela Andé, Ana-Maria Musina, Vivien Scipiceno, Christine Lagorce-Pepin, Fabienne Harmatta, Jérôme Galon, Jacques Flesch, Franck Paille
Now, your doctor can know your chances of survival very early and accurately.

This independent parameter has the highest relative contribution to the survival risk of all clinical parameters, including the TNM classification system.
Assess your immune response to maximize your survival chance

BEFORE

UP TO DATE

Your immune capital informs:

• If chemotherapy is needed for your personal case

• The efficient chemotherapy duration without unnecessarily altering your quality of life
Assess your immune response to tailor your chemotherapy

**STAGE II**
“can I avoid chemotherapy with no risk / peace of mind?”

**STAGE III**
« what is MY appropriate chemo duration without unnecessarily altering quality of life? »

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1. Pagès F et al. The Lancet 2018
With immunomics precision medicine

Paradigm change is underway

In treatment but also in prevention and control

Reveal your immune score:

- To better know your own cancer feature
- To avoid toxic unnecessary treatments
- To personalize your treatment
- To maximize your chance of survival
- To take part in your treatment decision making
Effective Clinical Experience

**Patient profile:**
67 Male diagnosed with T3 N0 sigmoid cancer lymphovascular and lymphatic invasion - some high risk features - ? chemo

Decided to use immunoscore® to help make decision.
Immunoscore® revealed – low risk of relapse -
Decision to not offer adjuvant chemotherapy.

**Patient profile:**
52 female diagnosed with T4 N0 transverse colon cancer - emergency presentation - ? Chemo

Decided to use immunoscore® to help make decision.
Immunoscore® revealed - high risk of relapse
Decision to offer chemotherapy