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REMARQUES : changements : 2 exercices supplémentaires cette année

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ABSTRACT WRITING

Table des matières :

I) Nivolumab plus chemotherapy versus chemotherapy alone

Fill the document while reading the article.

Introduction	
What is the background to the research?	4 study with safety data already exist. 2 study showed that nivolumab + chemotherapy improved progression free survival but not overall survival. 1 study revealed an improvement of overall survival. The last study did not showed a superior OS for patient with nivolumab and chemo
Why is this research important?	The first study to show a superior OS and PFS improvement Gastric cancer, including gastro-oesophageal junction cancer, is the fourth leading cause of cancer-relate deaths worldwide.
What is currently known about the topic?	Adenocarcinoma is the most common (>90%) histological type of gastric and gastro-oesophageal junction cancer. Fluoropyrimidine plus platinum-based chemotherapy, the most frequently used first-line treatment for unresectable advanced or metastatic human epidermal growth factor receptor 2 (HER2)-negative gastric and gastro-oesophageal junction adenocarcinoma.
What is unknown?	If chemotherapy + nivolumab might contribute to antitumour immune response elicited
Can you summarise the research question?	Can PD-1 inhibitor-based therapies associated with chemotherapy improve the treatment of previously untreated advanced gastric, gastro-oesophageal junction, or oesophageal adenocarcinoma ?
Methods	
Who was the target study population?	- 18 years or older - previously untreated, unresectable advanced or metastatic gastric, gastro- oesophageal junction, or oesophageal adenocarcinoma, regardless of PD-L1 expression. - Asia, australia, europe, North ans south America
Where/how were they enrolled?	**PD-L1 CPS of five or more based on results from the gastro-oesophageal cohort of CheckMate 032 and other published studies**

What are the eligibility criteria?	- measurable (at least one lesion) or evaluable disease per Response Evaluation Criteria in Solid Tumors (RECIST) - adequate organ function; and availability to provide a fresh or archival tumour sample to evaluate - previous adjuvant or neoadjuvant chemotherapy, radiotherapy, or chemoradiotherapy (administered at least 6 months before randomisation) - Excluded : HER2-positive status; untreated CNS metastases; peripheral neuropathy (higher than grade 1); active, known, or suspected autoimmune disease; positive test result for hepatitis B or C virus; and known history of positive test for HIV or known AIDS
How were patients allocated to groups?	- nivolumab + chemotherapy (XELOS or FOLFOX) - Nivolumab + ipilumab - Chemotherapy
What is the treatment protocol?	- nivolumab (360 mg every 3 weeks or 240 mg every 2 weeks) plus chemotherapy (XELOX [capecitabine 1000 mg/m2 twice a day, days 1–14 and oxaliplatin 130 mg/m2, day 1, every3weeks]orFOLFOX[leucovorin400mg/m2,day1, fluorouracil 400 mg/m2, day 1 and 1200 mg/m2, days 1–2, andoxaliplatin85mg/m2,day1,every2weeks]) - or chemo- therapy alone. - Intravenously except for capecitabine, which was administered orally. - Nivolumab was given for a maximum of 2 years. Chemotherapy was given per local standards.
What are the outcome measures?	OS Overall survival (time from randomization to death) and PFS progression free survival (time from randomization to the date of first documented tumor progression or death).
What statistical techniques are used?	final PFS and interim OS analyses to be assessed at 12-month minimum follow-up and final OS analysis at 24-month minimum follow-up
Results	
How many subjects were included?	1549 patients
What happened to all subjects?	received one or more doses of the assigned treatment: nivolumab plus chemotherapy (782 patients) or chemotherapy alone (767 patients)

What are the results for each outcome?	OS : - 13,1 months rivolumab + chemotherapy - 11,1 months chemotherapy alone 29% reduction in the risk of death PFS : - nivolumab + chemotherapy 7,7 months - Chemotherapy 6 months
What do the results say regarding the question?	The association of chemotherapy + nivolumab improved the treatment of previously untreated advanced gastric, gastro-oesophageal junction, or oesophageal adenocarcinoma ?
What is the most important result?	Significant improvement in OS
Conclusion	
What do the results seem to show?	The benefice of nivolumab + chemo instead of only chemotherapy
How should this affect medical practice?	Instead of only chemotherapy, we should add nivolumab
Were there any limitations?	On the basis of data available at the time of study design, tumour cell PD-L1 expression was chosen as a stratification factor for CheckMate 649. Following reports that indicated that PD-L1 CPS had better enrichment for efficacy than tumour cell PD-L1 expression in advanced gastric, gastro- oesophageal junction, and oesophageal adenocarci- noma, the protocol was amended to use expression of PD-L1 with a CPS of five or more to define the primary population. In addition, demographics and baseline disease characteristics were balanced between treatment groups in the population with a PD-L1 CPS of five or more. Patients with known HER2-positive status were excluded from CheckMate 649.
How does this affect the conclusions?	

II) How to write an abstract

Video on moodle : https://www.youtube.com/watch?v=lbCh94nJqIo

An abstract is a short and concise summary of a longer work such as a research paper. It's usually around 150 to 300 words. It should be a completely independent and self contained text, but not a copy.

There are four things to include in an abstract :

- research problem and objectives
- methods
- results
- conclusion

In the abstract, we see some important things : timing of the evaluation (baseline) and also, the main outcome : the orientation the authors chose to check the situation.

It's important to give precise numbers, one of them in particular : the number of patient who completed the study. It's something to remember -> Loss of follow up.

Then we have some results, p-value, etc : this is necessary in the results section ++. In the conclusion, they rephrase the main symptoms using the PAST.

Randomized study :
We have to make sure it's a randomized study, be careful of the details (1:1, 2:1…). We also have the flowtrack.
What is a doubleblind study ?
In theory, it was a double blind story because healthcare workers and patients were masked. But in real life, what happened ? In this study, what happened ? The thing is that ketamine has a strong taste (bitter), so, you will notice if you have been given ketamine. There's a way for the patients to know that they took ketamine : because of the taste and the effects (euphoria ++). So, double blind can be questioned.
It was a proof-of-concept (PoC) study. So there's no a lot of things to say about external validity ("is it applicable to general population ?"). Here, the answer would be no but it was not the aim of the study (interventional VS PoC here).
*"**We chose** to extrapolate the dosage from those described for intravenous administration"*
This is not ok for interventional (?) study ? Because in phase 3, we should decide which dose to use and it's not the case here.
*"tailor it based on **expected** oral absorption"*

Example :
Abstract group work

Title : Efficacy of a programmed cell death protein-1 inhibitors combined with chemotherapy for the first-line treatment of advanced gastric cancer

Introduction :
Adding a programmed cell death protein-1 (PD-1) inhibitor-based therapy to first-line chemotherapy such as nivolumab is known to improve the outcome of advanced gastric cancer. Nevertheless no direct comparison has been done to prove this protocole.

Methods :
Therefore an open label was conducted in 175 hospitals and cancer centrers in 29 countries across Asia, Australia, Europe, North America, and South America.

People aged 18 years old or older with previously untreated, unresectable advanced or metastatic gastric, gastro oesophageal junction, or oesophageal adenocarcinoma. Patients were randomly assigned to a group and then were administered nivolumab (360 mg every 3 weeks or 240 mg every 2 weeks) plus investigator's choice of chemotherapy or nivolumab plus ipilimumab versus chemotherapy alone.

Results :
A total of 2,687 patients were screened, and 1,581 were randomized to receive nivolumab plus chemotherapy (n=789) or chemotherapy alone (n=792), with 1,549 receiving treatment. The median follow-up for overall survival (OS) was 13.1 months for the nivolumab group and 11.1 months for the chemotherapy group. Most patients were non-Asian (76%) and had gastric cancer (70%). **Nivolumab plus chemotherapy** reduced the risk of death by 29% and improved median OS by 3.3 months in patients with PD-L1 CPS ≥5. Progression-free survival (PFS) and response rates were also better with nivolumab, though adverse events, including treatment-related deaths, were more frequent. The survival benefit of nivolumab plus chemotherapy was **consistent across various subgroup**

Discussion :
This study shows that the overall survival seems to improve in the nivolumab plus chemotherapy group.
Then Nivolumab should be included with chemotherapy to treat advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma.
However HER2 status was not known for everyone before the studies and people with positive HER2 were supposed to be excluded.
These results have led to approval in the USA and support nivolumab plus chemotherapy as a new standard first-line treatment.

Keywords: open label, randomisation, nivolumab plus chemotherapy or chemotherapy alone, reducing risk of death , progression free survival, first-line treatment

III) Tenses in an abstract/Quel temps utiliser dans quelle partie

(Elle n'en a pas parlé mais on laisse quand même ça peut servir…)

1. **Introduction/ Background**

= What is already known (background)

So I use present perfect

Ex: We have seen chronic IBS cases increase in recent years

= Why they did it

So I use past (and past passive)

Ex: This study was undertaken to discover the link between alcohol consumption and liver cancer.

2. **Material/Methods**

= What was done (detailed description)

So I use past / past passive

Ex: We conducted an open label trial in the Netherlands.

Ex: Adults were enrolled in the trial if they had informed written consent.

3. **Results**

=What was found

So I use past

Ex: There were 8 cases of alleviated blood glucose in 80 patients.

4. **Discussion**

= What is sure (significance and limitations)

So I use present

Ex: Cases of asthma decrease with age

Ex: The findings corroborate with the Study INCITE2

= What is possible

So I use modals (can, may)

Ex: Bias should have been minimalized

Ex: Patients may have had different reactions according to their gender

= What remains to be done (further research)

So I use "future/hypothesis"

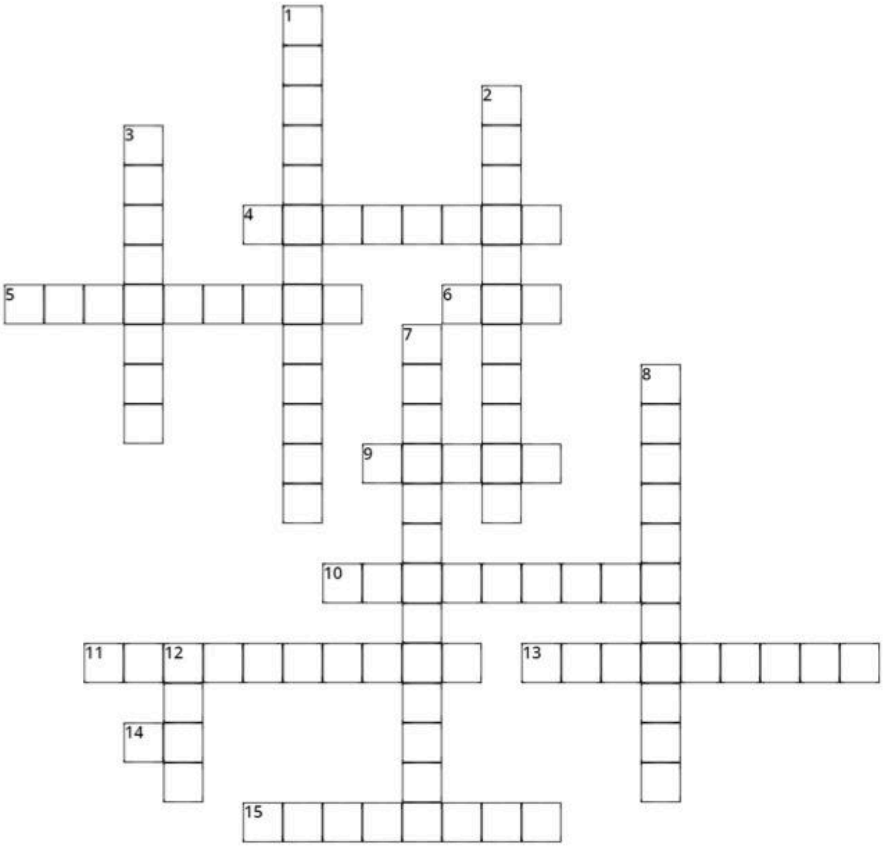
Ex: Further research could be made to explore the link between smoking and pregnancy defects.

IV) Crossword

Link to the article to complete the crossword :
https://www.medscape.com/viewarticle/conjugated-antibodies-emerging-star-ovarian-cancer-tx-2024a1000h56?form=fpf

Conjugated Antibodies: Emergin

https://www.medscape.com/viewarticle/conjugated-antibodies-e

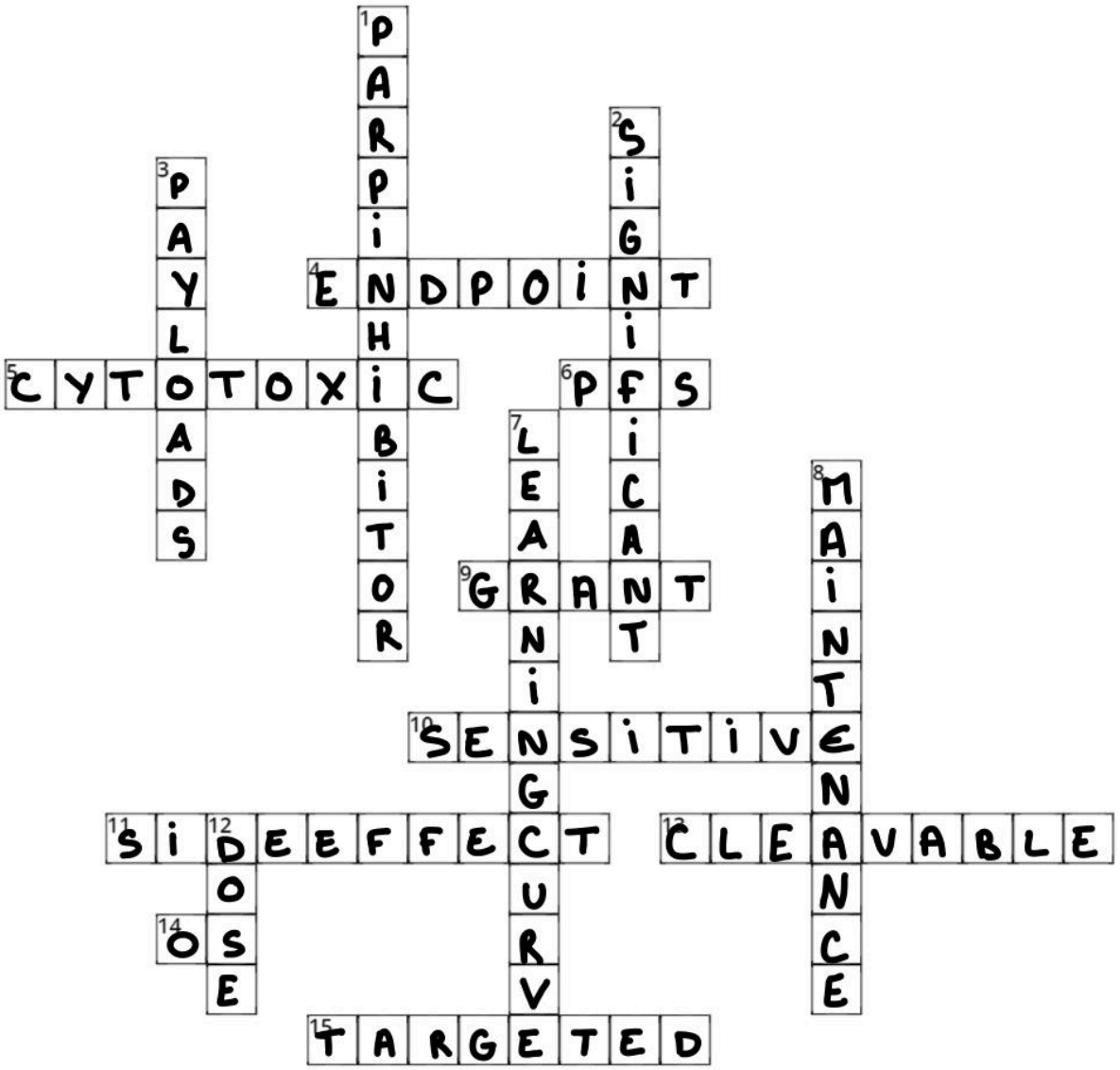


Horizontal

4. A primary goal or outcome measure in a clinical trial, used to determine the effectiveness of a treatment.
5. Referring to substances that are toxic to cells, particularly cancer cells; these drugs work by killing or damaging cells.
6. The length of time during and after treatment that a patient lives without the cancer getting worse.
9. A sum of money given by a government or other organisation for a particular purpose.
10. Describing cancer that responds well to treatment, such as chemotherapy or targeted therapy.
11. An unintended consequence or negative effect of a treatment that occurs in addition to its desired effects.
13. Capable of being broken apart; in ADCs, it refers to a linker that can separate the drug from the antibody inside the target cell.
14. The length of time from diagnosis or treatment start that patients are still alive, regardless of disease status.
15. Referring to therapies designed to specifically affect certain cells or molecules, often improving treatment

Vertical

1. A class of drug that blocks the PARP enzyme, used to treat certain types of cancer by preventing DNA repair in cancer cells.
2. Meaning important or notable; in clinical trials, it often refers to results that show a meaningful effect of a treatment.
3. The cytotoxic drugs delivered by an antibody-drug conjugate to kill cancer cells.
7. The process of learning skills by learning from mistakes
8. Ongoing treatment given after initial therapy to help keep cancer from returning.
12. The specific amount of a drug administered to a patient, often measured in milligrams or other units.



V) Last exercise

High-Dose Vitamin D Disappoints in Metastatic CRC: SOLARIS

Correct order :

Vitamin D has demonstrated anticancer properties, including inhibiting tumor growth and inducing cell death, in preclinical studies, and the phase 2 SUNSHINE trial found higher vitamin D levels improved progression-free survival in patients with advanced or metastatic CRC. The phase 3 SOLARIS trial aimed to confirm these findings.

The trial enrolled 455 patients with previously untreated, locally advanced or metastatic CRC. Patients had measurable disease and good performance status and had not been taking regular high-dose vitamin D over the past year. Patients had no preexisting hypercalcemia or any condition predisposing to hypercalcemia.

Participants were randomized to standard chemotherapy with FOLFOX or FOLFIRI plus bevacizumab with either high dose vitamin D3 (a loading dose of 8000 IU/d for 2 weeks, followed by a maintenance dose of 4000 IU/d) or to a control receiving 400-IU/d vitamin D3 (standard-dose group).

The two groups were well balanced, with no significant differences in demographics, tumor or treatment factors, or genomic alterations. After a median follow-up of 20 months, Ng and colleagues observed no statistically significant difference in progression-free survival between the two groups — a median of 11.8 months in the high-dose vitamin D group vs 10.3 months in the standard-dose group (hazard ratio [HR], 0.92; P = .25).

The researchers also reported no significant difference between the two groups in overall survival outcomes — a median of 25.6 months for the high-dose group vs 27.0 months for the standard-dose group (HR, 1.05; P = .34) — or in objective response rate — 51% for the high-dose group vs 44% for the standard-dose group (P = .12).

Subgroup analysis suggested a potential benefit for patients with left-sided primary tumors, where high-dose vitamin D was associated with a small but significant improvement in progression-free survival (HR, 0.74; interaction P = .015). This apparent benefit in patients with left-sided tumors required further study and confirmation, Ng said. However, "we should not jump into another clinical trial of vitamin D for left-sided patients until we better understand whether there's a biological explanation for it."

Ng noted that there is preliminary data from a separate study that suggested a possible higher expression of the vitamin D receptors in left-sided tumors than in right-sided tumors. The researchers also found no significant differences in grade 3 or higher adverse events between the two treatment groups, and compliance with vitamin D supplementation was high in both groups. In response to an audience question, Ng noted that baseline vitamin D levels were unknown in SOLARIS and in SUNSHINE.

"We know that almost all patients with metastatic colorectal cancer have baseline vitamin D deficiency, and we excluded those who likely were very sufficient based on prior high-dose vitamin D use in the year before study enrollment," she explained.

Given the positive results from SUNSHINE, SOLARIS was a "very good idea and it was well done," said the study discussant, Michel Ducreux, MD, PhD, with Gustave Roussy Cancer Center, Paris-Saclay University in France. Unfortunately, it's a completely negative trial, which is disappointing but also important, said Ducreux, who also did not think a new trial in left-sided tumors would be worthwhile.