UE : 17- Anglais

ENSEIGNANT : Riou

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REMARQUES :

REVISION CLASS

Table des matières

I- QCM socrative

1. Look at the image. What is this called?

- (A) pyramid of proof
- (B) pyramid of evidence
- (C) clinical practice guidelines
- (D) triangle of doom
- (E) progressive rating of study designs
- (F) none of the above

Réponse : B

2. Which study design is being described?

Study objective *- To identify and assess the contributions of major risk factors for campylobacteriosis in New Zealand.*
Design *- Home interviews were conducted over nine months using a standardised questionnaire to assess recent food consumption and other exposures.*
Setting *- Four centres in New Zealand with high notification rates of campylobacter infections-Auckland, Hamilton, Wellington, and Christchurch.*
Participants *- Case patients were 621 people notified between 1 June 1994 and 28 February 1995 as having campylobacter infection. Control subjects were selected randomly from telephone directories, and were matched 1:1 with case patients in relation to sex, age group, and home telephone prefix.*
Results *- Risk of campylobacteriosis was strongly associated with recent consumption of raw or undercooked chicken (matched odds ratio 4.52, 95% confidence interval 2.88, 7.10).*

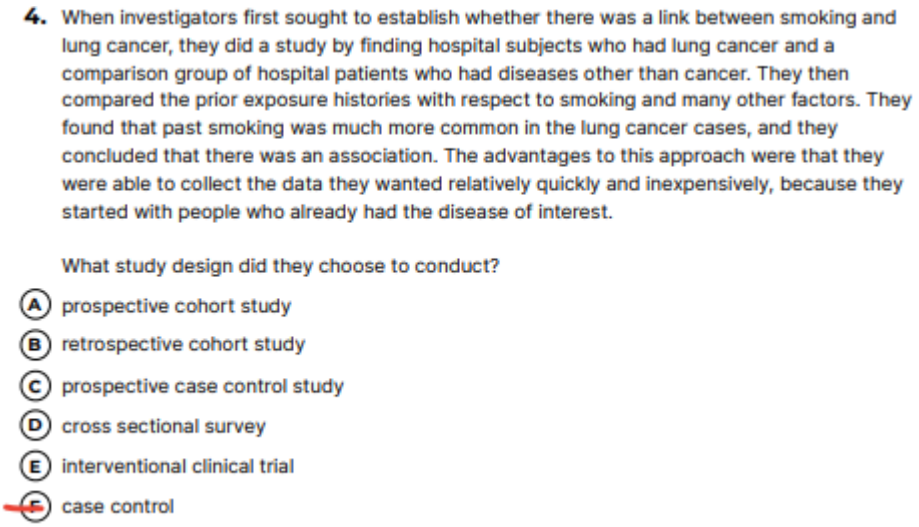
- (A) RCT
- (B) case control
- (C) meta- analysis
- (D) prospective case control case control is never prospective
- (E) case series
- (F) cohort

Réponse B

3. RCTs:

- (A) require blinding
- (B) are observational
- (C) require inclusion and exclusion criteria
- (D) must follow the IMRaD structure all research follow IMRaD
- (E) use a computer to randomize group allocation
- (F) are qualified using the impact factor
- (G) require a control group

Réponse CDEG


4. When investigators first sought to establish whether there was a link between smoking and lung cancer, they did a study by finding hospital subjects who had lung cancer and a comparison group of hospital patients who had diseases other than cancer. They then compared the prior exposure histories with respect to smoking and many other factors. They found that past smoking was much more common in the lung cancer cases, and they concluded that there was an association. The advantages to this approach were that they were able to collect the data they wanted relatively quickly and inexpensively, because they started with people who already had the disease of interest.

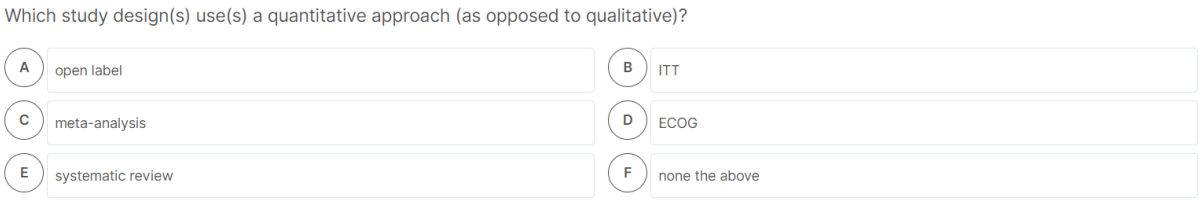
What study design did they choose to conduct?

A prospective cohort study
B retrospective cohort study
C prospective case control study
D cross sectional survey
E interventional clinical trial
F case control

:

Réponses F :

5 of 21


Which study design(s) use(s) a quantitative approach (as opposed to qualitative)?

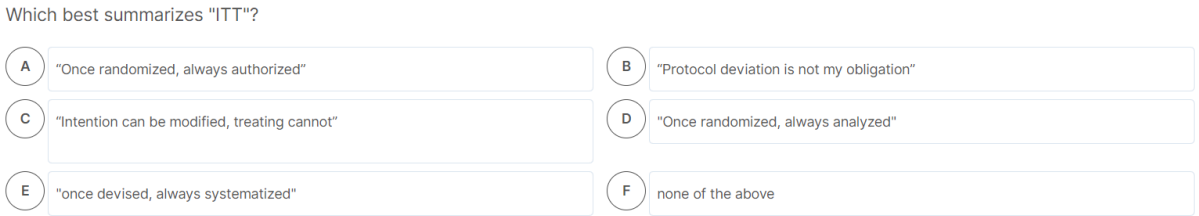
A open label
B ITT
C meta-analysis
D ECOG
E systematic review
F none the above

Réponse : C - meta-analysis

Remarques :

- open-label : everyone, patients et doctor know
- single-blind : only doctor knows
- double-blind : no one knows

6 of 21


Which best summarizes "ITT"?

A "Once randomized, always authorized"
B "Protocol deviation is not my obligation"
C "Intention can be modified, treating cannot"
D "Once randomized, always analyzed"
E "once devised, always systematized"
F none of the above

Réponse : D - “once randomized, always analyzed”

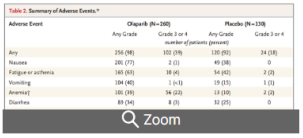
7 of 21

Complete the sentence:
"In a double-blind, placebo-controlled trial in Niger, we randomly assigned children who were 6 to 59 months of age and had uncomplicated severe acute malnutrition to receive amoxicillin or placebo for 7 days. The _____ was nutritional recovery at or before week 8."

A primary criteria
B evaluation criteria
C evaluation outcome
D primary outcome
E first outcome

Réponse : D - primary outcome (= primary endpoint)

8 of 21



Look at the table beside. How many participants in the control group suffered from fatigue or asthenia?

A 58
B 42
C 54
D 165

Table 2. Summary of Adverse Events.*

Adverse Event	Olaparib (N=260)		Placebo (N=130)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	number of patients (percent)			
Any	256 (98)	102 (39)	120 (92)	24 (18)
Nausea	201 (77)	2 (1)	49 (38)	0
Fatigue or asthenia	165 (63)	10 (4)	54 (42)	2 (2)
Vomiting	104 (40)	1 (<1)	19 (15)	1 (1)
Anemia†	101 (39)	56 (22)	13 (10)	2 (2)
Diarrhea	89 (34)	8 (3)	32 (25)	0

Réponse : C - 54

9 of 21

Which cancer(s) has/have no screening available

A pancreatic
B colorectal
C breast
D cervical
E lung

Réponse : A - pancreatic

10 of 21

Why is loss of follow up a problem in RCTs?

A it can lead to attrition bias
B Kaplan-Meier cannot be calculated
C FDA approval cannot be granted
D it can reflect poorly on the trial centre
E it can reduce the statistical power because group sizes may become unbalanced

Réponses : AE
Loss of follow-up can lead to attrition bias and can reduce the statistical power because group sizes may become unbalanced.

11 of 21

Drug X is used to treat a certain condition; it is currently administered over 12 months but can be administered for a shorter treatment period, which causes fewer side effects and is less costly. Which type of trial should you conduct to decide treatment duration?

A ITT
B non labeled
C superiority
D interventional follow up
E non inferiority

Réponse : E - Non inferiority

12 of 21

Complete the sentence:
"...the most common reason for noncompletion of the treatment regimen was the participant's decision to stop taking the trial drug. There were _____differences in demographic and clinical characteristics between participants who completed therapy and those who did not..."

A significant
B significative
C signifying
D significantly
E significants

Réponse : A - significant

13 of 21

The IF is calculated

A Using the number of citations quoted in a journal of a particular article
B over a 5 year period
C using the number of citations and articles of a particular journal
D by the NEJM, the Lancet and Nature
E to compare and assess research

Réponse : C - using the number of citations and articles of a particular journal, over a period of two years.

14 of 21

What does the acronym NSCLC mean?

Réponse : Non-Small-Cell-Lung-Cancer

15 of 21

a study was conducted to see the efficacy of an antiviral medication on complications of influenza. Patients included were 18+, with flu-like symptoms at the time of enrolment, without any history of allergy, asthma, COPD, or smoking.
What bias(es) need(s) to be considered?

A attrition bias
B selection bias
C correlation bias
D all of the above

Réponse : B - selection bias

16 of 21

In the analysis section of a research paper, what do the letters OR stand for?

A off response
B operating room
C odds ratio
D onset recruitment
E none of the above

Réponse : C - Odds ratio

17 of 21

internal validity

A considers attrition bias
B can be measured with the IF
C affects the reliability of results
D is considered appropriate when the statistical power of a study is above 80%
E all of the above

Réponse : AC
Internal validity considers attrition bias and affects the reliability of results.

18 of 20

Phase one clinical trials:

A	enroll volunteers with or without the condition under study	B	require large population samples
C	focus on the safety of the medical intervention	D	usually take years to complete
E	focus on compliance of participants to help for future studies	F	none of the above

Réponse : C

19 of 20

What is the NNT?

Number needed to treat

Réponse : Number needed to treat

20 of 20

Which study design(s) use both published AND unpublished data?

A	case reports	B	case controls
C	systematic reviews	D	randomized, controlled, superiority trials
E	randomized, controlled non-inferiority trials	F	meta-analyses
G	none of the above		

Réponses: C

II - Revision : abstract

Apixaban for the Treatment of Venous Thromboembolism Associated with Cancer
BACKGROUND
Recent guidelines recommend consideration of the use of oral edoxaban or rivaroxaban for the treatment of venous thromboembolism in patients with cancer. However, the benefit of these oral agents is limited by the increased risk of bleeding associated with their use.
METHODS
This was a multinational, randomized, investigator-initiated, open-label, **noninferior** trial with blinded central outcome adjudication. We randomly assigned consecutive patients with cancer who had symptomatic or incidental acute proximal deep-vein thrombosis or

pulmonary embolism to receive oral apixaban (at a dose of 10 mg twice daily for the first 7 days, followed by 5 mg twice daily) or subcutaneous dalteparin (at a dose of 200 IU per kilogram of body weight once daily for the first month, followed by 150 IU per kilogram once daily). The treatments were administered for 6 months. The **primary outcome** was objectively confirmed recurrent venous thromboembolism during the trial period. The principal safety **outcome** was major bleeding.
RESULTS
Recurrent venous thromboembolism occurred in 32 of 576 patients (5.6%) in the apixaban group and in 46 of 579 patients (7.9%) in the dalteparin group (**hazard ratio**, 0.63; 95% confidence interval [CI], 0.37 to 1.07; P<0.001 for noninferiority). Major bleeding occurred in 22 patients (3.8%) in the apixaban group and in 23 patients (4.0%) in the dalteparin group (hazard ratio, 0.82; 95% CI, 0.40 to 1.69; P = 0.60).
CONCLUSIONS
Oral apixaban was noninferior to subcutaneous dalteparin for the treatment of cancer-associated venous thromboembolism without an increased risk of major bleeding. (Funded by the Bristol-Myers Squibb–Pfizer Alliance; Caravaggio ClinicalTrials.gov number, NCT03045406.)

Adjuvant Olaparib for Patients with BRCA1- or BRCA2- Mutated Breast Cancer
BACKGROUND
Poly(adenosine diphosphate–ribose) polymerase inhibitors target cancers with defects in homologous recombination repair by synthetic lethality. New therapies are needed to reduce recurrence in patients with BRCA1 or BRCA2 germline mutation– associated early breast cancer.
METHODS
We conducted a phase 3, **double-blind**, randomized trial involving patients with human epidermal growth factor receptor 2 (HER2)–negative early breast cancer with BRCA1 or BRCA2 germline pathogenic or likely pathogenic variants and high risk clinicopathological factors who had received local treatment and neoadjuvant or adjuvant chemotherapy. Patients were randomly assigned (in a 1:1 ratio) to 1 year of oral olaparib or placebo. The primary endpoint was invasive **diseases-free survival**.
RESULTS
A total of 1836 patients underwent randomization. At a prespecified event-driven interim analysis with a median follow-up of 2.5 years, the 3-year invasive disease–free survival was 85.9% in the olaparib group and 77.1% in the placebo group (difference, 8.8 percentage points; 95% confidence interval [CI], 4.5 to 13.0; hazard ratio for invasive disease or death, 0.58; 99.5% CI, 0.41 to 0.82; P<0.001). The 3-year distant disease–free survival was 87.5% in the olaparib group and 80.4% in the placebo group (difference, 7.1 percentage points; 95% CI, 3.0 to 11.1; hazard ratio for distant disease or death, 0.57; 99.5% CI, 0.39 to 0.83; P<0.001). Olaparib was associated with fewer deaths than placebo (59 and 86, respectively) (hazard ratio, 0.68; 99% CI, 0.44 to 1.05; P = 0.02); however, the between-group difference was not **significant** at an interim-analysis boundary of a **p-value** of less than 0.01. Safety data were consistent with known side effects of olaparib, with no excess serious adverse events or adverse events of special interest.
CONCLUSIONS

Among patients with high-risk, HER2-negative early breast cancer and germline BRCA1 or BRCA2 pathogenic or likely pathogenic variants, adjuvant olaparib after completion of local treatment and neoadjuvant or adjuvant chemotherapy was associated with **significantly** longer survival free of invasive or distant disease than was placebo. Olaparib had limited effects on global patient-reported quality of life. (Funded by the National Cancer Institute and AstraZeneca; OlympiA ClinicalTrials .gov number, NCT02032823.)

Durvalumab after Chemoradiotherapy in Stage III Non–SmallCell Lung Cancer

BACKGROUND

Most patients with locally advanced, unresectable, non–small-cell lung cancer (NSCLC) have disease progression despite definitive chemoradiotherapy (chemotherapy plus concurrent radiation therapy). This phase 3 study compared the anti–programmed death ligand 1 antibody durvalumab as consolidation therapy with placebo in patients with stage III NSCLC who did not have disease progression after two or more cycles of platinum-based chemoradiotherapy.

METHODS

We randomly assigned patients, in a 2:1 **ratio**, to receive durvalumab (at a dose of 10 mg per kilogram of body weight intravenously) or placebo every 2 weeks for up to 12 months. The study drug was administered 1 to 42 days after the patients had received chemoradiotherapy. The coprimary end points were **progression-free survival** (as assessed by means of blinded independent central review) and overall survival (unplanned for the interim analysis). Secondary end points included 12-month and 18-month progression-free survival rates, the objective response rate, the duration of response, the time to death or distant metastasis, and safety.

RESULTS

Of 713 patients who **underwent** randomization, 709 received consolidation therapy (473 received durvalumab and 236 received placebo). The median progression-free survival from randomization was 16.8 months (95% confidence interval [CI], 13.0 to 18.1) with durvalumab versus 5.6 months (95% CI, 4.6 to 7.8) with placebo (stratified hazard ratio for disease progression or death, 0.52; 95% CI, 0.42 to 0.65; P<0.001); the 12-month progression-free survival rate was 55.9% versus 35.3%, and the 18-month progression-free survival rate was 44.2% versus 27.0%. The response rate was higher with durvalumab than with placebo (28.4% vs. 16.0%; P<0.001), and the median duration of response was longer (72.8% vs. 46.8% of the patients had an ongoing response at 18 months). The median time to death or distant metastasis was longer with durvalumab than with placebo (23.2 months vs. 14.6 months; P<0.001). Grade 3 or 4 **adverse events** occurred in 29.9% of the patients who received durvalumab and 26.1% of those who received placebo; the most common adverse event of grade 3 or 4 was pneumonia (4.4% and 3.8%, respectively). A total of 15.4% of patients in the durvalumab group and 9.8% of those in the placebo group discontinued the study drug because of adverse events.

CONCLUSIONS

Progression-free survival was significantly longer with durvalumab than with placebo. The secondary end points also favored durvalumab, and safety was similar between the groups. (Funded by AstraZeneca; PACIFIC ClinicalTrials.gov number, NCT02125461.)

III- Snakes and ladders game