Double-blind phase I-II clinical trials: preliminary risk analysis applied to the pharmaceutical circuit of injectable anticancer drugs in a preparation unit

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Background

- Approval for phase I-II clinical trials (CT) in our unit
- Increase in CT activity
- Good Preparation Practices (2022)

Process **H**azard **A**nalysis **(PHA)** : pharmaceutical circuit for injectable anticancer drugs used in phase I-II-III CTs in onco-hematology

Double-blind phase I-II CT (excluding placebo-controlled CTs, which follow a different process) : complex, as a high risk of exclusion is unblinding

Objective

Share the **corrective measures** drawn from our PHA, specific to these phase I-II CTs

Methods

Working group: 3 pharmacists
Clinical trials
Pharmacotechnics
Risk analysis

18 meetings (April 2023-May 2024) including 3 on double-blind, placebo-free phase I-II CTs

- Identification of **hazard situations**
- Evaluation of initial (iC) and residual (rC) **criticality**
- Implementation of **corrective measures**

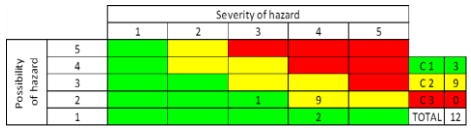
Results

3 phases
4 main risks
77 priority 1 HS

- Organizationnal
- Human
- Computer and technological infrastructures
- Technical

CT feasibility and computerized protocol drafting → 6 HS
Prescription → 4 HS
Preparation and control

10 priority 1 HS ➔ 12 scenarios élaborated



Initial criticality distribution

No hazard situation specific to double-blind, placebo-free phase I-II CTs identified for this phase

10 corrective measures grouped into 4 themes

Organization
Randomization sheet provided by CT team

Training
English-French lexicon terms related to CTs ; training sheet on the principle of double-blind CTs

Software configuration
Fictitious unit inaccessible to prescribers; standard wording allowing doses and INNs on the preparation sheet but not on the labels

Secure computer selection
Harmonization of computerized protocol wordings (CT name – INN/dose – Arm – Unique CT number)

DESTINY- CRC02 trastuzumab deruxtecan Bras 1 PHAR 904
DESTINY- CRC02 trastuzumab deruxtecan Bras 2 PHAR 904

Patient label

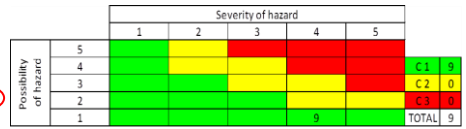
PHARMACIE HOPITAL SAINT ANTOINE - PARIS
I - IPP : le
Serv. : ESSAI CLINIQUES en fermé/ ONCO - Adm. le 05/0
TaLiOs-EN AVEUGLE nom de DCI invisible Tub
NaCl 0,9 % (Vol. : 100 mL), IV sur 1 H
TaLiOs essai protocole en aveugle Nom de DC
Conservation à 4° C
Péremp. le 06/01/2022 à 12:46
N° Ord.: 436 965
Liste I - RESPECTER LES DOSES PRESCRITES

Preparation sheet

Patient :		IPP	Né(e) le
Poids : 65 kg - Taille : 175 cm - S.C. : 1.79 m2 - Créat. : 0 µmol/L		Administration le 05/01/2022 à 12:37	
Dose prescrite	2 100,00 mg	(2 100,00 mg/1) sur 1 Jour(s)	
DCI :	TaLiOs-EN AVEUGLE nom de DCI invisible Tub filtre 0.2/ RO7247669 (PD1 LAG3		Matériel (traçabilité)
Protocole :	TaLiOs essai protocole en aveugle Nom de DCI invisibl	Sas : Hotte flux airla	Cycle 5 Jour : 1

Spécialité	Dosage	Numéro lot	Vol. (mL	Solvant	Vol à prélever (mL)	Dose utilisée
R07247669 (PD1-LAG3) IWRS	300,0	GLI0341-01 ; AH628140	6,00	Prêt à l'emploi	Totalité (6 mL)	300,00

After implementing our corrective measures, no scenario had a rC ≥ 2.



Residual criticality distribution

Discussion/Conclusion

The implementation of our corrective measures has allowed us to **make the risks acceptable** and to secure the phase I-II double-blind, placebo-free CT circuit in our preparation unit, especially in the critical preparation stage, by **computerizing the preparation sheet in Chimio® without removing the double-blind**.
Corrective measures established for **training** are essential and need to be regularly updated..

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