Course unit name: CLINICAL PHARMACOKINETICS OF ANTINEOPLASTIC DRUGS

1.- General information

Code	303008	Plan		ECTS	3
Type	Elective	Course	2023/2024	Periodicity	1st Semester
Department	Pharmaceutical Sciences				
Virtual Platform	Platform:	Studium:			
	URL de Acces:	https://studium.usal.es/			

Faculty

Professor coodinator	Dra. Amparo Sánchez Navarro		
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Professor	Dra. Maria José García Sánchez
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Professor	Dr. José Germán Sánchez Hernández		
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Professor	Dr. Paulo Roberto Teixeira Leite Lourenco Da Silva		
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2.- The course in the context of the Master´s Program

Treaning Module
Thirth block (out of six) of master program organization.

General aim of the subject
The objective of this subject is to review and apply the basic concepts of clinical pharmacokinetics (PK) together with "*in silico*" tools for optimization of the pharmacological treatment of cancer diseases. Clinical PK contributes to the precision medicine in personalising drug treatments according to patient charactristics . In addition, therapeutic drug monitoring (TDM) is addressed as a tool for dosage individualization to improve clinical outcomes in terms of efficacy and/or safety.

Professional specialization
This topic is oriented to researchers and clinicians involved in clinical investigation, drug development and improvement of antineoplastic drugs. These include pharmacists, , biologists, biotechnologists and other professionals integrated in multidisciplinary groups working on optimization of pharmacological treatment of cancer diseases.

3.- Previous recommendations

No specific requirements.

4.- Aims of the subject

To adquire theoretical and practical knowledge about antineoplastic drugs oriented to the study of its pharmacokinetics (PK) and the main factors responsible for PK variability.

To adquire the ability to apply "*in silico*" and TDM tools to incorporate PK variability for precision dosage in the clinical practice.

Specific aims:

- To know the mecanism of action of the main antineoplastic drugs used in the clinical practice
- To understand the population pharmacokinetic (PopPK) modeling and simulation methodology and the factors with a relevant impact on patient exposure to antineoplastic drug (demographics, phisiopathological, genetics, etc.)
- To study the concepts and tools regarding TDM of antineoplastic drugs in the clinical routine
- To learn about phisiological based pharmacokinetic (PBPK) modeling and simulations approach and its application to *in silico* clinical trials
- To achieve a holistic knowledge on the operation in a hospital pharmacy service for development, validation and follow-up of oncological therapies

5.- Contents

TOPICS (LECTURES):

1. Mecanism of action of the main anticancer drugs used in the clinical practice.
2. Clinical pharmacokinetics: basic concepts and application to antineoplastic drugs.
3. Population pharmacokinetics (PopPK).
4. Physiological Based Pharmacokinetic (PBPK) models.
5. Model-informed precision dosing and follow-up criteria in oncologyc treatments.

SEMINARS and HANDS-ON:

1. Data handling and Bayesian estimation.
2. Implementation of population pharmacokinetic models.
3. Parameters estimation of antineoplastic drugs: case reports.
4. Aplication of PBPK models to oncology patients.
5. *In silico* clinical trials.
6. Development and validation of the oncology therapy in a hospital pharmacy service.

6.- Skills to be acquired

Basic skills
Understanding the usefulness of clinical PK to evaluate factors with a significant impact on the response to pharmacological treatments. Capacity to apply dosage individualization tools in the oncological patient. Ability to use the PopPK models to improve the efficacy and safety of treatments with antineoplastic drugs. Ability to use the PBPK models for “first-in-human” dose estimation and dosage individualization.

Specific skills
- Interpretation and aplicacion of TDM results to optimize and individualize pharmacological treatments with antineoplastic drugs. - Using pharmacokinetic information to select the dosage regimen with the optimal benefit/risk ratio for antineoplastic drugs . - Ability to perform clinical trial in virtual populations. - Understanding the multidisciplinarity of the clinical team involved in the validation and follow-up of onco-hematolologic therapies.

7.- Teaching methodology

- Indroductory activity
- Lectures
- Seminars
- Hands-on
- Case reports discussions
- Focused activities: presentation, analysis and proposals related to scientific papers

8.- Estimated learning time

		Hours tutored by the teacher		Individual work (hours)	TOTAL HOURS
		Attendance required (hours)	Distance learning (hours)		
Lectures		11	8	10	29
Practices	- In classroom				
	- In laboratory				
	- In computer classroom	6			6
	- Countryside				
	- Visualization classroom				
Seminars		4		2	6
Work presentations and debates		8		7	15
Tutorials		2		2	4
Online activities					
Work preparation			5	7	12
Other activities		3			3
TOTAL		**34**	**13**	**28**	**75**

9.- Materials

Books

Individualizing Dosage Regimens of Antineoplastic Agents. In Individualized Drug Therapy for Patients: Basic foundations, Relevant software and clinical applications. Ed. Jelliffe R and Neely M. Elsevier. 281-306, 2017.

A First Course in Pharmacokinetics and Biopharmaceutics by David Bourne: **http://www.boomer.org/c/p4/**

Scientific Journals

- Therapeutic Drug Monitoring
- Clinical Pharmacokinetics
- British Journal of Clinical Pharmacology
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Recommended lecture

- Veal GJ, et al. Pharmacodynamic Therapeutic Drug Monitoring for Cancer: Challenges, Advances, and Future Opportunities. Ther Drug Monit;41:142–159. 2019
- Evan J. B & Paul K. L. A unified pharmacokinetic approach to individualized drug dosing. Br J Clin Pharmacol. 73:365-2125. 2011
- Guidi M, Csajka C, Buclin T. Parametric Approaches in Population Pharmacokinetics. J Clin Pharmacol. 2020 Oct 26. doi: 10.1002/jcph.1633. Epub ahead of print. PMID: 33103774. https://doi.org/10.1002/jcph.1633
- Darwich, A. S., Polasek, T. M., Aronson, J. et al. (2021). Model-Informed Precision Dosing: Background, Requirements, Validation, Implementation, and Forward Trajectory of Individualizing Drug Therapy. Annual Review of Pharmacology and Toxicology, 61(1), 225–245. https://doi.org/10.1146/annurev-pharmtox-033020-113257
- Tycho Heimbach, Wen Lin, Florence Hourcade-Potelleret, Xianbin Tian, Francois Pierre Combes, Nicholas Horvath, Handan He. (2019). Physiologically Based Pharmacokinetic Modeling to Supplement Nilotinib Pharmacokinetics and Confirm Dose

Selection in Pediatric Patients. Journal of Pharmaceutical Sciences 108: 2191-2198 https://doi.org/10.1016/j.xphs.2019.01.028

10.- Assessment

Assessments on the performance of the student
Continous follow-up of the capacities, abilities and knowledge adquired by the students. Student participation will be highly appreciated and positively taking into account. Attendence and active participation in lectures and seminars (hands-on). Comments and proposals to the case-studies. Scientific accuracy of the commentaries and answers to the questions. Presentation and debate of a scientific paper.

Recommendations
Active participation in the proposed activities. Debate about the multidisciplinarity of the oncological treatments.