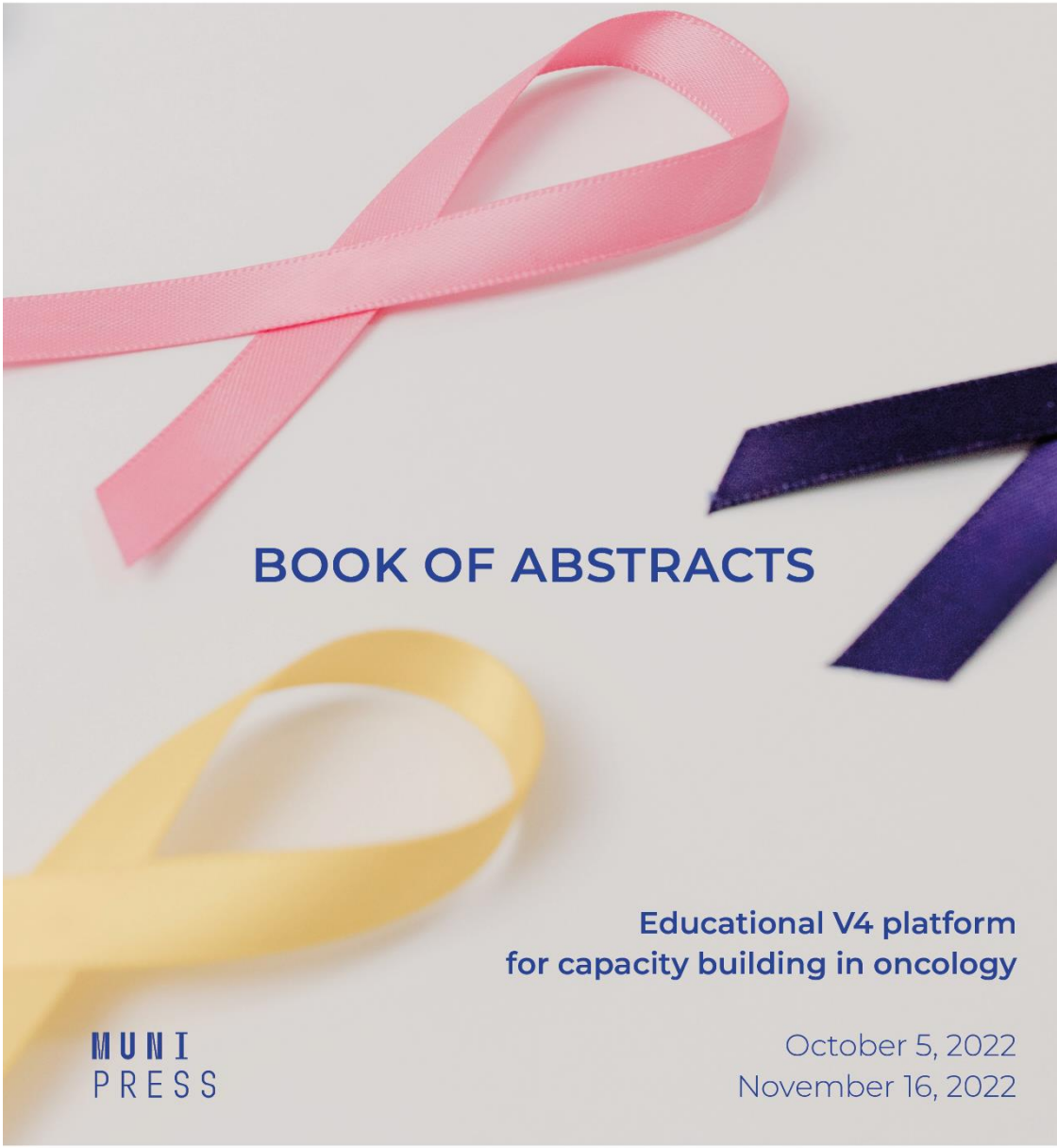

BOOK OF ABSTRACTS

Educational V4 platform for capacity building in oncology

October 5, 2022
November 16, 2022

Masaryk University
Brno, CZ, 2023
The training is supported by The International Visegrad Fund project No. #22120071, and from the state budget through MEYS, by the LRI CZECRIN project (LM2023049).

Book of abstracts Editorial Board:
Lenka Součková
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ISBN 978-80-280-0453-8

Content

Educational V4 platform

Foreword

The primary motivation of the authors of the educational workshop was to increase interest in involvement in clinical studies initiated in the academic environment. The education workshop is intended for all those interested in deepening knowledge in clinical management methodology studies, whether design aspects studies or data processing. A number of researchers determined to initiate clinical the study is often taken aback, and sometimes even from their intention (on the preparation of which they have already spent amount of time) repulsed when first confronted with by finding out what everything is administratively and legislatively conducting a clinical trial means.

The conduct of a clinical trial should be based on general principles of project management. One of the main art is so called Study team - participating workers as study coordinators, start-up managers, study nurses, on the implementation of the study at the place of its implementation, i.e., most often in a medical facility.

State of Art

The main issue is the very low capacity of specialized clinical trial coordinators, start-up managers, and nurses. We are

aware we were requested to change face-to-face to an online event that enables more participants and decreases expenses. However, the online form seems challenging in the current COVID world, where we are overwhelmed by online conferences and daily online meetings. Networking next to education was also the original intent of this project. Therefore, we prefer to organize one onsite, All-In-One educational event. The main objectives are to support educational activities and create a training center for study coordinators of clinical trials in oncology, which complement and build the capacity of research staff to meet international clinical research practices compliant with Good Clinical Practice. The main obstacles to conducting non-commercial clinical trials are enormous administrative workload, study costs, and the low capacity of professionals as coordinators and study nurses, leading to a small number of academic investigator-initiated trials in V4. According to a survey conducted by the Association of Innovative Industries (AIFP), prepared by Ernst and Young in 2019 for the Czech Republic, most clinical trials are in Oncology and Immunology, making more than half of all trials. Compared to 2015, the number of clinical trials increased significantly by 56% in Oncology in the Czech Republic in 2019. The growing trend of increasing the number of clinical trials in oncology concerns the entire V4 region.

Methodology

For cooperation between hospitals, specialized workplaces, and clinical trial sponsors, the key is to set up appropriate processes and effective communication through trained specialists - clinical trial coordinators, without whom clinical trials, especially in oncology workplaces, would no longer be feasible. The targets are: alleviate the shortage of study researchers by trained study coordinators and study nurses; increase the interest in academic clinical research among physicians and other research staff; enhance efficiency and save the time of professional staff through training and workshops in created training centers; support the education and training of postgraduate students and professionals, including internships; increase knowledge or awareness of clinical trial procedures and standards in those countries, and support the training and exchange of information for the regulatory representatives and EC members within the countries, including internships. The main contribution of all partners is the basic idea and its implementation of the following work packages that help achieve the objectives: WP1 – Clinical trial management training in oncology (Good Clinical Practice, Informed Consent Forms, Protocol, Investigator Brochure, etc.); WP2 - Oncology clinical trial training; WP3 – Education in biostatistics and analysis (planning of protocol, statistic design, statistical analysis plan; WP4 – Pathology and molecular biology in clinical trials design.

Capacity building

This goal was achieved partly during the project period as this part of the planned results will be mostly realized in the next two years.

As there is a promotional strategy, we will work with partners to have the toolkits linked to adequate institutional webs and other E-sources. as the V4 E-learning platform have a broad reach, we assume that more than partner institutions will use the developed tool. The direct implementation into institutions' websites is complicated due to security policies and rules, but PharmAround will be continuously working on spreading the information about the availability of this tool. Off-line promotion at workplaces employing employees of the target group - LF MU Brno, partner organizations - rollups in their facilities Off-line presentation at target group gathering places - a promotion at professional events focused on clinical evaluation - PharmAround event - a meeting of nurses and clinical trial coordinators. Studies - Brno, September 2023, 2024- approx. One hundred sixty experts, a National day of clinical evaluations - Prague, May 2023/2024, under the auspices of Ministry of Healthcare, PharmAround conference - October 2023/2024, inclusion in the CZECRIN Academy - cooperation with a partner specialized in clinical evaluations. There will always be a promotion in the program (prepared graphics) during the events (rollups, video banner/slide) and short information in the program. Note from us to the main objective of this project: building capacity: In general, clinical research network capacity building refers to programs aimed at enhancing networks of researchers to conduct clinical research. Although a large body of research exists in the literature on developing and building capacity in clinical research networks, the conceptualizations and implementations remain controversial and challenging.

Primary objective

The Educational V4 platform is forming a new academic V4 countries network within selected comprehensive cancer centers. In the Educational V4 platform, the planned V4 level of e-learning material and curriculum will meet the needs of our target groups – clinical trial coordinators, biomedical students (medical-oncology, pharmacy, clinical research master) towards having a very unique and socially beneficial career via an innovative online, work-based, multidisciplinary learning model. This output is considered an outstanding added value at the V4 level and beyond through activities carried out in all participating project partners and organizations in Research Infrastructure Networks. The Educational V4 platform is innovative because there is a training strategy for clinical trial researchers in V4, but no medical training for clinical research coordinators has been developed yet. It takes the challenge to develop a curriculum and e-learning material for coordinators and biomedical students in undergraduate programs with the assistance of PHARMAROUND Network – MOÚ, SLOVACRIN, Centrum Onkologii Poland, and Dél-Pest Centrum Kórház. The general objective of the Educational V4 platform is to tackle the skills gaps and mismatches related to the V4-level Clinical Oncology Trial. As another is innovative mark is developing online infrastructures to coordinate these multi-partner international programs.

Education

The training is to support early-career of study coordinators or nurses in oncology and to strengthen a basic clinical trial oncologist

skills and expertise while providing the possibility to present trainee skills and gained knowledge during the training.

Each work package takes in total of 4 hours and contains theoretical and practical parts. Theoretical part is an expert part with presentations. Practical part contains quiz, quick question, Q&A. Every attendee who completes this training will receive a Certificate of Attendance.

The whole training was promoted through our PHARMAROUND webpages, conferences, email invitations, and online invitation. The way and result of this training will be applied similarly in all participating oncology institutes. The GDP process could be applied over all connected V4 institutes united with the WP CHAIN OF FOUR promotion. Slightly changes should always respect the local laws and customs of the V4 countries. Promotion of the training seminar was mainly conducted through direct channels – an offline promotion at events and email communication. Due to the high demand for participation, the event's capacity was soon filled, and there was no room for further activities. The aim was to keep the number of participants at a level that would allow the seminar to be interactive and allow discussion for all participants. When capacity was reached, we decided to move the promotional activities to the second phase of the project – the maintenance phase. A web sub-site has been established for the project and is now a supporting platform for all event materials. Among other things, social networking sites (Facebook and LinkedIn accounts) have been set up, which will be used mainly in the future to promote the materials and recordings of the event. The plan to use newsletters for online communication and promotion via individual partners' websites is under discussion.

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Project funders and consortium

Project funder and guarantor

The VISEGRAD FUND

The International Visegrad Fund is a donor organization established in 2000 by the governments of the Visegrad Group countries – Czechia, Hungary, Poland and Slovakia. The Fund follows the vision of President Vaclav Havel, President Lech Wałęsa and Prime Minister József Antall and supports regional cooperation of civil society organizations. That is possible thanks to Grants, Scholarships and Artists Residencies. They seek original approaches that help the region progress in seven main areas of Culture, Education, Innovation, Democratic Values, Public Policy, Environment and Tourism, and Social Development. Source: https://www.visegradfund.org/about-us/the-fund/

PHARMAROUND Endowment Fund

The PharmAround Endowment Fund was founded in January 2015. Its activities build on a successful project called Clinical Evaluations and Pharmacology for 3rd Millennium - a Multimodal

PharmAround Educational Platform, which was carried out by the Faculty of Medicine at Masaryk University in Brno in 2011-2014.

The aim of the endowment was to create foundations for mutual co-operation and education in the field of drug development to raise awareness of this issue among students of medicine, professionals and general public. Thus, a system involving universities, secondary medical schools, health care facilities, pharmaceutical companies and also professionals in the fields of regulation of drugs or research and development has been set up.

Project consortium – Partners

Masaryk Memorial Cancer Institution

Masaryk Memorial Cancer Institute (MMCI) in Brno is a specialized comprehensive cancer center with a supra-regional activity that is certified by two quality certificates – by Joint Commission International (JCI) and Joint Accreditation Commission of the Czech Republic (SAK ČR). The institute concentrates on all essential branches of medicine to ensure complex oncological care, including prevention, epidemiologic, diagnostics, and particular modalities of cancer treatment and physiotherapy. Focusing on research and scientific activities, the institute is also involved in the pre-gradual and post-

gradual education of doctors and other healthcare professionals and popular science activities aimed at the broad public. Annually, almost 10000 patients are hospitalized in the institute, and 200000 people pass through the ambulatories.

Pavol Jozef Safarik University in Kosice, the Faculty of Medicine

Pavol Jozef Safarik University in Kosice supports preparing and implementing academic clinical trials in Slovakia, including international trials. University has a proven track record in developing and delivering innovative, collaborative education programs, including Ph.D. programs for scientists and clinicians and professional development courses for academic researchers and industry professionals. University uses a novel and innovative online infrastructures to coordinate these multi-partner programs. The National Oncology Institute (NCI) in Slovakia provides comprehensive oncological care at the highest professional level and performs consulting services in oncology for oncological workplaces in Slovakia to provide preventive care. The NCI Department of Clinical Studies has provided professional support to clinical research at the NCI for 25 years.

Centrum Onkologii – Instytutu im. Marii Skłodowskiej-Curie

Oncology Center – Institute of Maria Skłodowska-Curie is currently the largest oncology facility in Poland, consisting of three departments: Warsaw, Gliwice, and Krakow. Oncology centrum experts have outstanding knowledge of planning and data analysis of clinical research and bioinformatics and biostatistics methodologies that support evaluating the human clinical trial process. Their experts have experience setting up, leading, and managing genomics and bioinformatics core facilities, supporting researchers with standardized bioinformatics and scientific computing services. Oncology experts have actively taught and targeted training courses in biostatistics, bioinformatics, and programming for biomedical students and researchers. At present, we have no joint projects, but the MOU hospital is in the connection concerning biostatistics.

Dél-Pest Centrumkórház

Dél-Pest Centrumkórház is one of Hungary's largest oncology centers, where patients have access to the anti-tumor therapies available in our country, and many clinical drug trials take place.

The oncology department of Szent László Hospital was founded in 1998. At the request of the former heads of the institute, anti-tumor treatments started in the hospital with a room designated for outpatient treatment and three wards with 12 beds. Today, this department - as the oncology center of the United Szent István and Szent László Hospital, later known as the Dél-Pest Centrumkórház - is one of the leading oncology healing, professional and scientific centers in the country.

Educational V4 platform support

Czech Clinical Research Infrastructure Network CZECRIN

CZECRIN is the key infrastructure supporting the implementation of academic clinical research in the Czech Republic. CZECRIN, as the national node of Clinical Research Infrastructures of the European Network ECRIN-ERIC, makes a fundamental contribution to academic institutions' involvement in international clinical research projects. LRI CZECRIN was built as a unique infrastructure involving the network of most major clinical sites with a focus on clinical research and providing knowledge, development, production, and implementation capacities in the research and development of drugs and medical devices. CZECRIN set up advanced solutions for effectively provisioning and using high-quality scientific data, fully implementing the FAIR (Findable, Accessible, Interoperable, and Reusable) principles. CZECRIN is also a center for education in clinical trials.
Source: https://czecrin.cz/en/home/

Slovak Clinical Research Infrastructure network

SLOVACRIN is the national hub for non-commercial clinical trials in Slovakia and has been part of the European ECRIN-ERIC consortium since 2018. It represents a national distributed research infrastructure connecting hospitals, universities, and scientific institutions involved in academic clinical research across the Slovak Republic. The Faculty of Medicine of the Pavol Jozef Šafárik University in Košice, UPJŠ LF coordinate SLOVACRIN. UPJŠ LF is also the host institution of the European Correspondent. The national infrastructure aims to increase the number and quality of academically initiated clinical trials in Slovakia, using the available capacity and expertise, knowledge, research, and development in the field of medical sciences and building a network of Clinical Trials Units (CTUs) that can provide support for the actual implementation of clinical trials. Establishing a network of national clinical trial units in healthcare institutions is essential and crucial for conducting clinical research.
Source: https://slovacrin.sk/en/about-us/

The National Cancer Institute (“NCI”)

The National Cancer Institute (“NCI”) is a specialized hospital facility focused on providing comprehensive medical oncological care in the scope of specialized outpatient health care, specialized institutional health care, standard examination and treatment units, and intensive health care in the relevant medical fields. NCI provides comprehensive oncological care at the highest professional level, performs conciliar services in oncology for oncology centers in the Slovak Republic territory, and provides preventive care.

Source: https://www.nou.sk/en/mission-of-nou

Organizing and scientific committee

Organizing Committee

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Hana Vladíková, Bc., BBA

Jiří Deml, MD

Andrea Holomková, MSc

Scientific Committee

Radka Lordick Obermannová, Assoc. prof. MD, Ph.D.

Regina Demlová, Assoc. prof. MD, Ph.D.

Programme

October 5, 2022, from 8 am ending 5 pm
8:00 – 8:15 Welcome, Agenda and Technical issues

WP 1 Clinical trial management

8:15 – 9:05
Introduction to clinical trials management – basic Principles and rules, roles and competencies, reporting, and related documents (including Informed Consent Forms, Protocol, Investigator brochures, Medical Reports, Case Report Forms, Etc.). What is important to know for a study coordinator or start-up manager? *(Beata Čečetková)*

9:05 – 9:25
Communication in clinical trial management *(Simona Sonderlichová)*
9:25 – 9:55
Basic pharmacovigilance principles and rules *(Radka Troníčková)*
9:55 – 10:15
Clinical trials in Slovakia – country example *(Daniela Světlovská)*
10:15 – 10:30
Coffee Break (15 minutes)

Workshop: "*The practical performance of different phases of clinical trials in oncology within hospital settings.*"

10:30 - 12:30

Responsibilities, competencies, and delegation (Start-up management, Delegation logs, training, communications, and other respective topics). *(Martina Lojová, Hana Blahynková, Simona Sonderlichová)*

12:30 – 13:10

Lunch Break (40 minutes)

WP 2 Clinical trial in Oncology

13:10 – 13:30 Part I

TNM Classification, CTCAE *(Radka Lordick Obermannová)*

13:30 – 15:00 Part II

Basics about cancers
Breast cancer *(Michal Chovanec)*
Gastrointestinal tumours – colorectal, pancreas, biliary tract tumours *(Éva Végh)*
Genitourinary tumours *(Michal Chovanec)*
Lung cancer *(Simona Bořilová)*

Coffee Break will be part of the Skills part

Workshop: *"How to select the right patient for the right trial."*

15:00 – 17:00

Short examples of patients' medical reports and clinical trials' inclusion criteria to guide the selection of the right trial for the right patient. *(Daniela Světlovská, Radka Obermannová, Šárka Selvekerová)*

November 16, 2022, from 8 am ending 5 pm
8:00 – 8:15 Welcome, Agenda and Technical issues

WP 3 Education in biostatistics and analyzes

8:30 – 9:20

Statistical aspects of clinical trials for non-statisticians *(Adam Svobodník)*

9:20 – 9:30
Discussion
9:30 – 10:20

Endpoints in clinical trials and time-to-event data *(Iveta Selingerová)*
10:20 – 10:30
Discussion
10:30 – 10:40 Coffee Break (10 minutes)

Workshop: *"Statistics applied in clinical trials. How to read published results of clinical trials? "*

10:40 – 12:40

One of the main points is the basic knowledge of using biostatistics in clinical trials of study coordinators, start-up managers, and study nurses CZ *(Adam Svobodník, Iveta Selingerová)*.

12:40 – 13:00

Lunch Break (20 minutes)

WP 4 Pathology and molecular biology in clinical trials design

13:00 – 13:35

Biomarkers in oncology – medical oncologist's perspective *(Eva Vegh)*

13:35 – 14:10

The role of pathologist in clinical research *(Pavel Fabian)*

14:10 – 14:45

Basics of molecular biology in clinical research *(Petr Müller)*

14:45 – 15:00

Discussion

15:00 – 15:10

Coffee Break (10 minutes)

Workshop: *"How to use some molecular and genetic tools related to clinical research."*

15:10 – 17:10

Clinical interpretation of pathology reports & biomarkers *(Dr. Regő Szollosi)*

Different biomarkers for different tumours *(Radka Lordick Obermannová, Šárka Selvekerová)*

Molecular biomarkers and clinical applications *(Petr Müller)*

Abstracts

Workpackage WP1 – Clinical trial management

The unique package includes the GCP training, covering the main GCP principles for the investigators/coordinators and other staff involved in clinical trials at the hospital/site level. The scientific package includes processes and ways to write and create medical documents such as Informed Consent Forms, Protocols, Investigator Brochures, Medical Reports, Case Report Forms, etc. The pharmacovigilance package covers basic pharmacovigilance principles, rules, and reporting in clinical trials. According to the project/clinical study, the Regulatory package enables the students to implement the international and national regulatory rules for clinical trials (submission, follow-up, reporting to regulatory authorities, ethics committees, and other respective authorities). The execution package covers the practical performance of different phases of clinical trials in oncology within hospital settings.

Introduction to clinical trials management

Beata Čečetková
SLOVACRIN, Faculty of Medicine of the Pavol Jozef Šafárik University in Košice, Slovakia

Clinical trials are among the types of research projects that evaluate safety and efficacy of new drugs or vaccines. Thanks to the clinical trials, new innovative medicines and treatments are brought to patients. Similarly, clinical trials of medical devices provide new treatment and diagnostic options in a wide range of therapeutic areas.

In the context of so-called Evidence Based Medicine (EBM), clinical trials are the ultimate proof of evidence in practice. Only meta-analyses of these studies are considered above [Bencko et al., 2003]. Every innovative product that is intended to be marketed, whether a drug or a new medical device, must undergo a clinical trial.

Conducting a clinical trial requires both the enormous enthusiasm of the scientists and physicians involved, but also a very high budget. It is not always possible for academics, physicians and scientists to obtain sufficient grants to enable the research project to be carried out. The field of clinical trials (research on human subjects) must comply with a demanding and very strict regulatory process [ICH GCP (R2), 2016]. Often, it is this demanding and very specific process that represents a major barrier to project implementation. During clinical

trials, great requirements have to be met to maintain the safety of the subjects, not only those enrolled in the research, but also for the patients who might benefit from the treatment subsequently. In doing so, it is not crucial whether the research is carried out by large pharmaceutical companies or by an academic infrastructure, or directly by doctors in a healthcare facility. They all have to meet the same regulatory, administrative, and implementation conditions, which aim to maximise the safety of the subjects in the trials and the quality of results.

Communication in clinical trial management

Simona Sonderlichová
SLOVACRIN, Faculty of Medicine of the Pavol Jozef Šafárik University in Košice, Slovakia

Purpose of review: The purpose of the review is to provide basic rules in communication in clinical trial management.

Recent findings: Effective communication in clinical trial management is vitally important and is one of the key factors. Clinical trials involve many different teams working together, so communication skills are essential. Several questions need to be asked, such as: which persons are involved, the methods and the purpose of the communication, and the clinical trial lifecycle. The most suitable communication method depends on who is being communicated with, the purpose of that

communication, and the receiver's preferences. Communication methods may vary depending on the subject of communication. Effective communication has a key impact on the selection of a country/center in a clinical trial, the design of the clinical trial, and the conduct of the clinical trial itself.

Summary: Effective communication saves much time, but on the other hand, poor communication can cause misunderstandings and serious problems later on. It is essential to know the internal and external processes and to identify a contact person in each organization involved in the clinical trial.

Basic pharmacovigilance principles and rules

Radka Troníčková
TWMA Clinical Research and Pharmacovigilance, Prague, Czech Republic.

Purpose of the training: to introduce basic pharmacovigilance principles and rules in clinical trials.

Summary: The aim of pharmacovigilance is supervision of a medicinal product to ensure its maximum safety and best possible risk-benefit ratio. Pharmacovigilance includes the collection of information relevant to the safety, its evaluation and the implementation of appropriate measures. Safety must be continuously monitored throughout the whole life cycle of

the medicine including all phases of clinical trials. Pharmacovigilance information collected during clinical trials: adverse events, adverse drug reactions, serious adverse events, SUSARs – suspected unexpected serious adverse reactions and other events specified by clinical trial protocol. Adverse event is assessed with regard to its causality (relationship with IMP or study procedure), seriousness (according to seriousness criteria given by regulation), severity (graded intensity) and expectedness (consistency with reference safety information). Investigator is responsible for immediate reporting of serious adverse events to sponsor. Sponsor is responsible for expedited reporting of SUSARs to Eudra Vigilance and periodic reporting of Annual Safety Reports to Competent Authorities. Other reporting obligations are specified by EU/local regulations.

Clinical trials in Slovakia – country example

Daniela Světlovská
National Cancer Institute (NCI) in Bratislava, Slovakia

The legislative setting within Slovakia (Ministerial Order No. 4/2018) enables professional organizational and administrative support for clinical research. Ministerial Order No.4/2018 have incorporated clinical trial and biomedical research organizational units as a standard part of healthcare facilities. Inclusion is possible, but reflecting e.g. the financial

and personnel capabilities of individual medical facilities is not mandatory. In order to speed up the conclusion of clinical research contracts with medical facilities, a limit is set for responding to the draft contract and also in Annex no. 1 to the Minister's Order No. 4/2018 effective from 1.6. 2019 is a complete draft of the contract between the client and the medical facility.

The order was based on input (Ass. Prof Drgoňa, prof Mego) and also on almost 25 years (since 1995) of experiences and the work of the Clinical trials department at National Cancer Institute Slovakia (Dr Světlovská, Bc. Krieschová, Mrs. Jančíková, Mrs. Turňová...) and with support of Slovak Health Authority (MSc. Kováčová), National Oncology Institute (NOI) (Dr. Rečková), Slovacrin (Dr. Čečetková) and other important professionals in the field of clinical research and with thanks to Institute of Research of Development of Ministry of Health (DR. Kvietiková).

Only 3 months after the order was issued, 12 departments of clinical trials and 7 departments of biomedical research were established in Slovakia.

Challenge remains to create a catalog of work activities for clinical research coordinators, which could favorably support research activities in this area.

Responsibilities, competencies, and delegation

Martina Lojová[1], Hana Blahynková[1], Simona Sonderlichová[2]
[1] Masaryk Memorial Cancer Institution, Brno, Czech Republic
[2] SLOVACRIN, Faculty of Medicine of the Pavol Jozef Šafárik University in Košice, Slovakia

Education part under motto: "*The practical performance of different phases of clinical trials in oncology within hospital settings*".

Participation of the Study Coordinator or study nurses implementing the study is already commonly practiced in most healthcare facilities, which participate more regularly in clinical trials. Although their job content and specific responsibilities may vary between institutions, ideally, it consists of a coordinator/organizational nurse, information, and administrative background for the entire study team. Within the competence of the coordinator/the study nurse may, therefore, also have an obligation to promptly and correctly distribute relevant information from the Protocol to other study team members.
The examiner is responsible for implementing a clinical study at the place of its implementation (the so-called trial site). If the difficulty of the study requires it, it helps him ensure the necessary activities, a team of other qualified persons - studying or solving team. It can then apply to individual members of the study team chief examiner to delegate part of

his duties. The delegation of individual duties must be in accordance with the professional qualifications of the members of the study group team. On the other hand, delegation is essential for increasing efficiency in implementation studies because it will allow doctors to concentrate on their own "clinical" work and thus avoid being overwhelmed with administrative activities.
The workshop briefly describes the organizations of the start-up process at Masaryk Memorial Cancer Institute. The primary responsibilities were described, and practical skills were tested by creating a relevant study team to a specific protocol. In addition, participants were asked to draft a delegation protocol for that protocol.

Summary: Based on the questionnaire results (performed before the training) and discussion outputs received after that, it was obvious that some issues regarding the correct filling of the delegation log are complicated and may have multiple interpretations. The discussion with the participants, who were start-up coordinators, study coordinators, nurses, and data managers with different lengths of experience, was very fruitful, pointing out some national and institutional differences and possible scenarios to overcome some discrepancies were presented.

Workpackage WP2 - Clinical trial in Oncology

WP2 workshop will take a total of 4 hours and will be divided into two-hour parts. The first two hours will be dedicated to lectures and seminars that cover the diagnosis and treatment of common solid tumors, i.e., tumors with high incidence, namely breast, colorectal, lung cancer, and another diagnosis gastric and kidney cancer, and malignant melanoma. The role of target therapy and new checkpoint inhibitors will be explained. The second part will be dedicated to skills. Participants will actively work on the selection procedure focused on" how to select the right patient for the right trial." During this second part, a physician experienced in oncology and principal investigator of academic and non-academic trials, and an oncology study coordinator will help participants acquire clinical research skills in oncology. Physicians educated in oncology will work as a tutor and introduce all diagnoses mentioned above, and their treatment Study coordinator educated in oncology will deliver together with investigator the active part of the seminar. All presentations will be available online. All training outputs will also be available for all participants.

TNM Classification, CTCAE, ECOG, RECIST

Radka Lordick Obermannová
Masaryk Memorial Cancer Institution, Brno, Czech Republic

TNM Classification of Malignant Tumors (TNM) is a standard classification system for identifying the extent of the spread of cancer. It applies to all solid tumours except leukaemia and central nervous system tumours.

TNM was developed by Pierre Denoix between 1943 and 1952, using the size and extension of the primary tumour, its lymphatic involvement, and the presence of metastases. Further, it was maintained by the Union for International Cancer Control (UICC). And in 1987, the UICC was unified with the American Joint Committee on Cancer (AJCC) staging system into the single TNM staging system.

TNM is a notation system that describes the stage of cancer using alphanumeric codes: T describes the size of the original (primary) tumour and whether it has invaded nearby tissue; N describes regional lymph nodes that are involved, and finally M means distant metastases. pTNM is dedicated to postoperative TNM staging and ypTNM is used in case of previous neoadjuvant or preoperative treatment. In the case of complete resection without positive margins, the term R0 is applied, R1 means microscopically positive margins, however, R2 means macroscopically positive. Once the TNM was set up

there are no changes allowed. In case of disease progression or relapses of cancer, the term rTNM is used.

Common Terminology Criteria for Adverse Events classification (CTCAE) were developed by the National Cancer Institute (NCI) of the United States of America. It is a regularly updated classification system that provides standards for reporting the severity of adverse events occurring in cancer clinical trials and clinical practice.

There are two widely used scoring systems to assess functional status: The ECOG Performance Status Scale (PS) and the Karnofsky Performance Status Scale (KI). Both scales describe a patient's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working, etc.). This helps oncologists identify suitable patients for clinical studies, but both scales are also an important part of our daily clinical practice. Every oncologist sets up PS or KI at the beginning of treatment and reevaluates and adapts regularly during treatment.

The Karnofsky index with a scale between 100 and 0, was introduced in a textbook in 1949 and ECOG performance status with a scale between 0 and 5 first appeared in the medical literature in 1960.

The presentation explains the above-mentioned terminology.

BASICS ABOUT CANCER, Breast cancer

Milan Chovanec
National Cancer Institute (NCI) in Bratislava, Slovakia

Breast cancer is one of the most common cancers. One in eight women will suffer from this disease during the lifetime. Risk factors include estrogen exposure, sex, age, benign lesions of breast, genetic factors, race and ethnicity as well as life-style. While novel molecular profiling led to recognizing distinct subtypes of breast cancer, clinically relevant remain hormonal positive, HER-2 positive and triple negative breast cancer. Treatment of early stage breast cancer aims for curative intent with surgery, adjuvant radiotherapy and adjuvant systemic therapy. Among the risk factors for relapse, the most important is nodal involvement. Advanced disease remains an incurable disease and represents the therapeutic dilemma. While metastatic breast cancer is a chemotherapy, hormone sensitive or anti-HER-2 sensitive disease, eventually treatment is exhausted in all patients and these succumb to their disease. Therefore, research initiatives are imperative in finding key data to overcome treatment resistance in breast cancer. Translational Research Unit at National Cancer Institute is designed for such purpose and serves an intersection for clinical and basic research.

Gastrointestinal tumours

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Purpose of review: The purpose of the review is to present the aetiology, the epidemiology, the diagnostic measures and the different treatment of the gastrointestinal malignancies (gastric, pancreatic, colorectal cancer, esophageal and biliary tract cancers also rare GI cancers etc.) also malignant melanoma.

Summary: GI cancers account for about 25% of cancer incidences globally and 35% of all cancer-related death. Some type of polyps can turn into cancers but it takes years. In addition to the imaging techniques (X-ray, ultrasound, CT, MR PET etc.) and endoscopy biopsy and histopathological examination are the basis for establishing the correct diagnosis. Optimal (curative) cancer surgery involves complete removal of the malignant tumour along with surrounding tissue and regional lymph nodes also restoring the function. Metastasectomy (liver, lung etc.) is common in colorectal cancer. Palliative surgery is performed when complete tumour removal is not feasibly but this type of surgical intervention can restore the function of the GI tract. Neoadjuvant/adjuvant radiotherapy of rectal cancer is able to reduce the local recurrence rate. Systematic anticancer treatment can be

neoadjuvant, adjuvant or palliative (first, second, third etc. line). Different doublet-triplet chemotherapy (contains fluorouracil, irinotecan, oxaliplatin, taxans etc.) also targeted therapies (for example bevacizumab, panitumumab, cetuximab, trastuzumab etc.) are used in GI cancers. Some immuno-oncological drugs are also effective in GI cancers (pembrolizumab, nivolumab, atezolizumab). Malignant melanoma develops from melanocytes (uveal, mucosal, skin). Breslow depth and Clark levels are important in staging. In recent years the emergence of effective immune and targeted therapies (BRAF inhibitors in combination with MEK inhibitors) in the adjuvant and palliative treatment of MM has changed the outcome of this aggressive disease.

Genitourinary tumours

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Genitourinary cancers include prostate, urothelial, kidney, adrenal and testicular cancer. Patient centered and high-quality management requires multidisciplinary care involving genitourinary oncologist, urologist, radiologist, radiotherapist, pathologist and intensive care specialist. Advances in the field of oncology led to substantially improved outcomes in treatment of genitourinary cancers. Whether it is simple rearrangement of existing treatments to castration sensitive

phase of prostate cancer, or implementing novel drugs or drug combinations in prostate, renal and urothelial cancer, the overall survival benefit achieved over the past decade is eminent. Testicular germ cell tumors are unique among other malignancies. These tumors are exceptionally sensitive to cisplatin-based chemotherapy with 95% long term cure rate. However, physicians and researchers are unable to unravel the underpinnings of cisplatin resistance in small group of patients dying from this disease. Innovative drugs deliver small to none treatment effect. Therefore, one priority of our department and Translational Research Unit is to research biomarkers, find novel therapies and discover underpinnings of late toxicity in testicular cancer.

Basics about Basics in Lung cancer

Simona Bořilová
Masaryk Memorial Cancer Institution, Brno, Czech Republic

Although lung cancer is placed second regarding incidence, is the leading cause of cancer-related mortality, with a 5-year survival rate of only 20% worldwide. This unfortunate first place is due to many reasons. Firstly, the majority of patients are diagnosed between 70 and 80 years of age, meaning the treatment is often complicated by patients' frailty and comorbidities. Secondly, as nearly half of lung cancer cases are diagnosed in the metastatic stage, there are limited

possibilities for a curative approach. 90 % of all lung cancers are caused by smoking.

Regarding the histopathological type, there are two main types of lung cancer: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), which is more common (about 80% of lung cancer cases). NSCLC can be subdivided into three different types: Adenocarcinoma, Squamous cell carcinoma, and Large cell carcinoma. Staging of lung cancer is performed by chest, abdomen, and pelvis CT scans, or in patients with a curative approach, PET/CT is preferred for better assessment of mediastinal lymph nodes. In these patients also, brain lesions should be ruled out through brain CT or MR. Tissue for histopathological analysis is usually obtained through bronchoscopy, percutaneous biopsy under the CT control, or by surgery.

The treatment of NSCLC depends on the stage. For local stages, resection, when feasible, is the golden standard. When surgery is not feasible either due to patient fitness or technical reasons, definitive radiotherapy could be offered to patients with sequential or concomitant chemotherapy, depending on patient performance status. In a metastatic setting, the treatment decision is subject to molecular testing, particularly in adenocarcinoma, where nowadays, there is testing for ALK, ROS-1 fusion, and EGFR mutation in a reflex manner. In cases with genetic alterations, the patient should be treated with

targeted therapy according to mutation. For patients without genetic alterations, the decision-making process is based on PD-L1 expression and overall performance status. According to the level of PD-L1, we can treat patients with immunotherapy (PD-1 or PD-L1 inhibitors) alone or in combination with platinum-based chemotherapy.

Short examples of patients' medical reports and clinical trials' inclusion criteria to guide the selection of the right trial for the right patient

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Workshop WP2 "How to select the right patient for the right trial ". Short examples of patients' medical reports and clinical trials' inclusion criteria were presented to guide the selection of the right trial for the right patient.

By completing three different exercises, we clarified the main inclusion and exclusion criteria and practiced how to search the source documentation. Afterward, the participants went through the questionnaires to control and explain the right solution for this training. A ten-item questionnaire was developed to assess the effectiveness of the lesson. Participants were asked to complete the questionnaire before and after the course. The questionnaire results showed that

participants understood the presented issues and could interpret them further.

Workpackage WP3 - Education in biostatistics and analyzes

The WP3 intended to provide an overview of the primary statistical and data analyses associated with oncology. It was planned for 4 hours. Presentations included Statistical aspects of clinical trials for non-statisticians and endpoints in clinical trials and time-to-event data. The educational part opened discussion about different types of hypotheses from superiority, non-inferiority to equivalence and bioequivalence. Special attention was drawn to focusing on definition of intention-to-treat and per-protocol analysis sets as this is of high importance in clinical trials in oncology. P-value concept and fundamentals of power analysis were discussed to provide insight into calculation of number of patients needed to be enrolled in clinical trials. During interactive workshop, selected manuscripts of published oncology clinical trials will be reviewed and discussed. Special attention will be paid to statistical section of the manuscripts with description of statistical methods applied. Results of the selected published clinical trials will be reviewed and interpreted with special focus on the difference between clinically and statistically significant findings

Statistical aspects of clinical trials for non-statisticians

Adam Svobodník
Masaryk University. Faculty of Medicine, Department of Pharmacology. CZECRIN

The lecture will be focused on basic statistical principles of clinical trials. Classification of trials from first-in-human studies through Phase I-IV studies will be presented and basic statistical methods applied in individual phases of clinical trials discussed. Fundamental terminology covering randomization, interim analysis, subgroup analysis, and meta-analysis will be reviewed. Different types of hypotheses from superiority, non-inferiority to equivalence and bioequivalence will be deconstructed. Special attention will be focused on definition of intention-to-treat and per-protocol analysis sets as this is of high importance in clinical trials in oncology. P-value concept and fundamentals of power analysis will be discussed to provide insight into calculation of number of patients needed to be enrolled in clinical trials.

Endpoints in clinical trials and time-to-event data

Iveta Selingerová
Masaryk Memorial Cancer Institution, Brno, Czech Republic

Clinical trials are an integral part of modern oncology, and thanks to the results based on clinical trials, it is possible to achieve progress in the treatment of cancer. To achieve relevant results, the clinical hypothesis, patient cohort, and study objectives must be properly formulated before the initiation of a clinical trial. The educational lesson is focused on clinical trials from a statistical point of view. Basic terminological concepts and their interrelationships in the planning and subsequent evaluation of clinical trials will be explained. The focus is on endpoints in clinical trials and their clinical and statistical types, such as binary outcomes or time-to-event endpoints. A considerable part of the lecture is devoted to time-to-event data, which are crucial components of clinical trials in oncology. A special field of statistics, survival analysis, is focused on this data. The introduction of necessary concepts from this area is also included. In the subsequent workshop, real clinical trials with their methodology and main published results will be discussed.

“Statistics applied in clinical trials. How to read published results of clinical trials? “

Adam Svobodník[1], Iveta Selingerová[2]

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During interactive workshop, selected manuscripts of published oncology clinical trials were reviewed and discussed. Special attention was paid to statistical section of the manuscripts with description of statistical methods applied. Results of the selected published clinical trials were reviewed and interpreted with special focus on the difference between clinically and statistically significant findings.

Workpackage WP4 - Pathology and molecular biology in clinical trials design

This WP4, Pathology and molecular biology in clinical trials design, was designed to apply molecular biology and genetics principles and technologies in oncology clinical and translational research. The WP provided basic concepts and principles of biomarkers in oncology from a medical oncologist‘s perspective; 2) The role of the pathologist in clinical research; 3) the Basics of molecular biology in clinical research. Training and career development programs provided skills training called “How to use some molecular and genetic tools related to clinical research. Trainees were practicing a clinical interpretation of pathology reports & biomarkers, Biopsy requisition forms and molecular biomarkers, and clinical applications. The topics covered the human genome, genomic variation, gene structure, gene expression, gene therapy, molecular diagnostics, and personalized/precision medicine. The skills part is named “How to use some molecular and genetic tools related to clinical research”. Training and career development programs provided opportunities for trainees to conduct supervised clinical and biological research to extend their research skills, for example, in Biopsy requisition form and test their knowledge in Molecular biomarkers and clinical application

Biomarkers in oncology – medical oncologist' perspective

Eva Végh
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Purpose of review: The purpose of the review is to present the role of biomarkers in cancer treatment and different types of these markers. Biomarkers can be found in blood, other bodily fluids and tissues

Summary: Better understanding of tumor pathophysiology and discoveries in molecular biology lead to an important new concept, the personalized medicine (tailored treatments, precision medicine). Tumors that originate in the same organ can have extremely different genomic drivers. Nowadays many cancers can be divided into special subgroups based on the tumor molecular characteristics. Biomarker testing may help to choose proper cancer treatment for each particular patient. Drug development entered a new era with development of targeted therapies and launching immune-oncological drugs. Predictive biomarkers play important and decisive role in the drug development process. Site agnostic treatments represent an important breakthrough ins cancer treatment. In most cases the companion diagnostic assay (CDx) is developed parallel to the drug. Tumor heterogeneity is a significant challenge in the implementation of targeted

therapies into routine because heterogeneity can lead to the formation of different cancer cell groups with other molecular characteristics, can seriously affects also the result of biomarker testing and the prognosis of patients. It is also important to emphasize that in the recent years the cost of sequencing (also NGS) has declined, and it can help to set up precise diagnoses and treatment plans for malignant diseases.

The role of pathologist in clinical research

Pavel Fabian
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The presentation focuses on Legal aspects of pathology, pathology in practice methods step by step including analytics (diagnostic pathology, molecular pathology), pre-analytics and post-analytics. Important part is also dedicated to special issues concerning clinical trials.

A part of the presentation was focused on the basic principles of histopathological diagnostics, including tissue fixation, histo-processing, paraffin embedding, sectioning, and staining. Other methodologic approaches are discussed, esp. immunohistochemistry, in situ hybridization, and DNA-based molecular pathology. The formalin fixation details (formalin concentration and pH, fixation time, cold ischaemia period time, etc.) and their impact on following laboratory procedures

are particularly interesting. Another emphasized area is TNM classification, its principles, rules, and other classification systems like ICD-O. Tumor tissue response after neoadjuvant therapy is explained at the same time with tumor regression grading systems (which reflect the therapy-related changes within the tumor tissue).

Basics of molecular biology in clinical research

Petr Müller
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Presentation was focused on the basic principles of tumour formation and the description of genetic changes leading to malignant transformation. The lecture aims to show that the knowledge of the molecular basis of tumour formation is the key to developing effective and targeted therapy. The transformation of a somatic cell into a tumour cell is caused by mutations in DNA that allow the cell to divide uncontrollably, activate growth signaling and proteosynthesis, make the cells immortal, and activate angiogenesis and metastasis. Therefore, several genetic changes, which we call driver mutations, are required to activate all tumour cell's properties. The basic condition for the formation of tumours is, therefore, an increase in the probability of the occurrence of mutations, which can be caused either by external mutagens or by the inability of the cell to repair mutations. Impairment of genes responsible for DNA repair leads to genomic instability, which increases the likelihood of mutations in other genes driving the malignant transformation. In terms of function, mutated genes can be divided into two basic groups, comprising oncogenes and tumour suppressors. Oncogenes refer to those genes whose alterations cause gain-of-function effects, while tumour

suppressor genes cause loss-of-function effects that contribute to the malignant phenotype.

"How to use some molecular and genetic tools related to clinical research."

The purpose of the workshop WP4 was to explain the role of biomarkers in daily medical practice and its effect on treatment decision.

Clinical interpretation of pathology reports & biomarkers

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A pathological report is crucial to transferring essential information between the oncologist and the pathologist. In everyday clinical practice, the best prognostic factor to define cancer recurrence is the TNM system. A biomarker is a functional biochemical or molecular indicator of a biological or disease process with predictive, diagnostic, and/or prognostic utility.

Predictive biomarkers are used in everyday clinical decisions to conclude the benefit of treatment to the patient and play an important role in drug development. With the use of predictive

biomarkers, we can avoid the toxicities of useless cancer treatment and limit the financial burden of expensive, ineffective therapy.

Molecular biomarkers and clinical applications

Petr Müller

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A key approach for revealing the genetic changes responsible for malignant transformation is tumour DNA sequencing. Next-generation sequencing (NGS) makes it possible to detect mutations in hundreds of genes at once and to identify mutations useful for determining prognosis and response to treatment. NGS can also reveal the mechanisms of mutagenesis and determine the total mutation load that can be used for the indication of immunotherapy.

Task examples:

1. Give an example of an oncogene and describe its function.

2. Give an example of one tumour suppressor and describe its function.

3. Find the most common genetic changes associated with colorectal cancer.

4. Give an example of a targeted antitumor therapy targeting a specific genetic alteration.

5. Give an example of gene amplification in tumours and methodical possibilities for its assessment.

Educational V4 platform for capacity building in oncology

Book of Abstracts

Editors: Hana Vladíková, Lenka Součková
Publisher: Masaryk University, Žerotínovo nám. 617/9, 601 77 Brno
Edition: 1., electronic, 2023
ISBN 978-80-280-0453-8

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