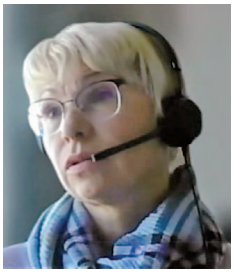
The current issues of the ethical review system in Ukraine in the context of Russian invasion



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1. Introduction

I am grateful, first of all, to the Japan Association of Bioethics, its representative Director Professor Chiaki Kagawa, and personally Professor Chieko Kurihara for such a great opportunity to present information about the ethical review system of Ukraine and the influence of war on our system. In addition, I am grateful to Francis Crawley for his willingness and initiative to support clinical trials in Ukraine during this devastating time, and his great energy, spent time, and brilliant ideas. I want to note and say my warmest greetings to the DIA team, especially Courtney Granville, for the opportunity to use the DIA platform during all of the summer of 2022. We can share and discuss different issues in clinical trials which arise during Russian aggression in Ukraine.

2. Regulatory authority of clinical trials in Ukraine

Ukraine is a huge European country (Fig. 1). The population is more than 41 million, but Ukraine is a low middle income country. It is GDP per capita in 2021 was only $2,500. It is not bigger GDP, so it is very important to spend this money in a proper way for health care support and development. If we find some good ways to involve other finances for our healthcare system for supporting our patients to give them some new medicines and modern treatment, it is very good, because current health expenditure as a share of GDP in 2019 was only 7% according to WHO publications. This 7% includes out-of-

Fig. 1　Ukraine snapshot - some facts about country and health care system

pocket money and government budget money for different medical provision. Therefore, we need additional support for our healthcare system and for the treatment of our patients. That is why clinical trials as one of such additional sources of proper support for our Ukrainian healthcare system are very important.

If we speak about the regulatory authority of Ukrainian clinical trials, it is the Ministry of Health of Ukraine. The state enterprise, "State Expert Center of the Ministry of Health of Ukraine", performing expertise assessment, approving all protocols of clinical trials in Ukraine.

3. Clinical trial status in Ukraine before the active invasion

How were clinical trials before this active war invasion in Ukraine? At the beginning of the active invasion of Russia on 24th February 2022, there were 794 clinical trials in the Ukrainian clinical trials enterprise, and all these clinical trials had been approved by the State Expert Center of the Ministry of Health of Ukraine and our Research Ethics Committees. Then, they were approved by our regulatory authority – Ministry of Health. 584 clinical trials had started and were being conducted in different phases: first, second, and third phase. Nearly 85-90% of these clinical trials were from international organizations and international sponsors, so they were multicenter clinical trials, and their sponsors were international companies. As of 24th February, 210 clinical trials had been approved by the Ministry of Health and were being prepared for their launch. The launching of clinical trials is a time-consuming process. So, all these clinical trials were prepared, clinical sites were ready, contract research organizations were prepared to conduct these clinical trials at that moment.

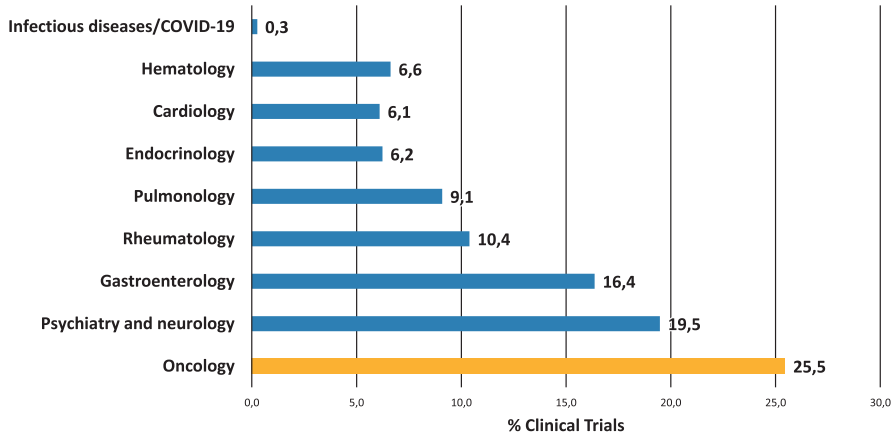
I want to emphasize that our State Expert Center has been very active since the first day of the war. Persons who have participated in the DIA webinars know that Dr. Taisa Herasymchuk, Director of the Department of expertise of materials for preclinical and clinical trials, presented these data, and presented the work of our State Expert Center. On the first day of this devastating situation, we did not know what to do with researches, patients, documentation, etc., but from the first week of March, our State Expert Center started finding solutions to support our clinical trials, to help our investigators, to help our sponsors, contract research organization, and offered different important decisions for clinical trial research subjects.

4. Distribution of clinical trials

Today, I will not speak about investigator-initiated clinical trials, but I will speak most of all about clinical trials, which are sponsored by pharmaceutical and biomedical companies like commercial clinical trials (Fig. 2). Investigator-initiated clinical trials are called "clinical research", not "clinical trial". It means that these researches are not interventional research. In such investigator-initiated clinical trials in Ukraine, we do not study non-registered, non-approved medicines. We will not speak today about such research. This is another topic for discussion, and it is much more about how medical science in Ukraine works. This topic needs other materials.

Today, I will draw your attention to only clinical trials which are sponsored by pharmaceutical and biomedical companies. The reason why we speak so carefully and why we pay huge attention to clinical trials in Ukraine is that 25% of these clinical trials are oncological clinical trials. During these clinical trials, drugs that are very important for humanity are studied, and this information is very important in terms of the activ-

Fig. 2　Distribution of clinical trials to nosology (2021) *



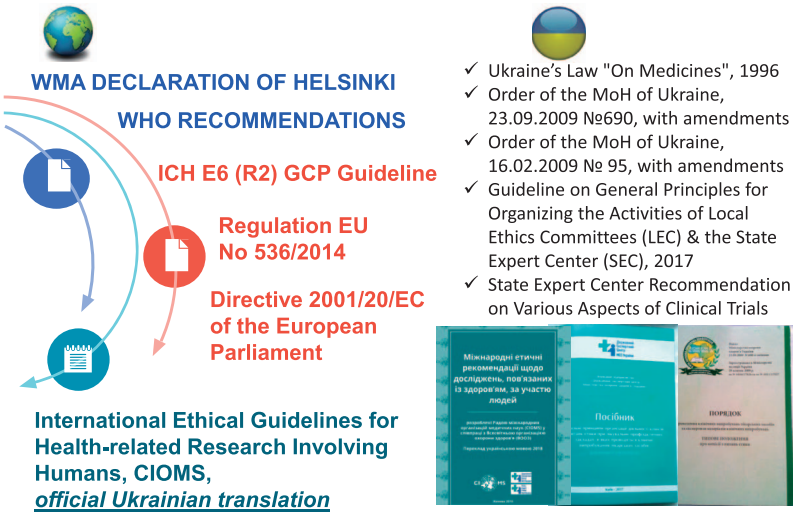
* according to data of State Expert Center Ministry of Health of Ukraine (https://www.dec.gov.ua/materials/aktualna-informacziya/?role=applicant)

ity, efficacy, and safety of these drugs. Therefore, you see how clinical trials in Ukraine are distributed according to nosology: psychological, neurological, gastroenterology, rheumatology, pulmonology, endocrinology, cardiology, and hematology diseases. This is the main field of our clinical trials in Ukraine. So, data from these researches are very important not only for Ukrainian patients but also for many patients who are enrolled and for many pharmaceutical companies and for healthcare professionals.

5. Normative and legislative documents

In Ukraine we work with all important basic normative documents of the European Union and world documents such as the Declaration of Helsinki, WHO recommendations, and CIOMS guidelines (Fig. 3). We use all these documents for the review of clinical trials in Ukraine. We have used these documents for the last

Fig. 3　Basic normative and legislative documents for Ukrainian clinical trial system



two decades. During the last two decades, our system of clinical trials has developed, and many new documents were added or some of these documents were changed. So, there are a lot of documents that are completely harmonized with European Union documents and with world documents for approval for assessment of clinical trials. So, Ukraine completely goes in the way of the European Union and the whole world according to the protection of human rights, and the quality of clinical trials is very important for us, for researchers: for sponsors, ethics committees, and our Ministry of Health and State Expert Center.

Therefore, we have, first of all, Ukraine's Law "On Medicines" (1996) and two main orders: Order of the Ministry of Health of Ukraine №690 with amendments (since 23.09.2009), Order of the Ministry of Health of Ukraine №. 95 (2009). These orders are amended, and these orders completely involve all topics in the ICH-GCP. Since 2021 , our State Expert Center has been included as an Observer (official status) in ICH and obtained the status of an Associate Member of the ICMRA (International Coalition of Medicines Regulatory Authorities). It is very important for collaboration and future harmonization of our system.

Again, I am presenting you information, which was designed by Sergii Rasputniak, head of GCP and GLP Audit Department of State Expert Center. Our Ukrainian Law of Medicines includes two articles, Article 7 and 8, about clinical trials of medicines and the protection of patient and volunteer's rights, who want to participate in clinical trials. Our main orders which regulate our clinical trials are the same. They include main topics and procedures which are in Directive 2001/20, so they are oriented with this document. ICH Good Clinical Practice Guidelines in Ukraine are all amended according to the R2 of the ICH GCP (E6).

I want to emphasize that in Ukraine the clinical studies approval process is a parallel process. The State Expert Center and local REC make a review and take decisions independently and approximately at the same time. So, our authority makes its own review of clinical trials, and our local REC makes its own review of these clinical trials. When both of them give their approvals, only then the clinical trial is started.

6. Research ethics review system in Ukraine

In general, the research ethics system in Ukraine can be described as a decentralized system with a lot of local RECs (Table 1). More than 400 local RECs exist in Ukraine. For participation in clinical trials as Research Center, each clinical trial site must have a working Research Ethics Committee. The US calls them the Institutional Review Board, but we call them Research Ethics Committees (RECs). Ukraine does not have central ethics committee. Therefore, local RECs are completely independent and have self-management. This is neither good nor bad. This is our local situation. A very interesting and very important point is that par-

Table 1 Research Ethics Review system in Ukraine

DECENTRALIZED SYSTEM:
•More than **400** local Research Ethics Committees at each trial site
•NO central ethics committee
•Most of REC's members are employees of institutions that have clinical trial sites
•Participation in REC is voluntary and non-payment duty
•Regulatory recommendation for researchers and sponsors from the **State Expert Center of the Ministry of Health of Ukraine** is a main informational source for RECs

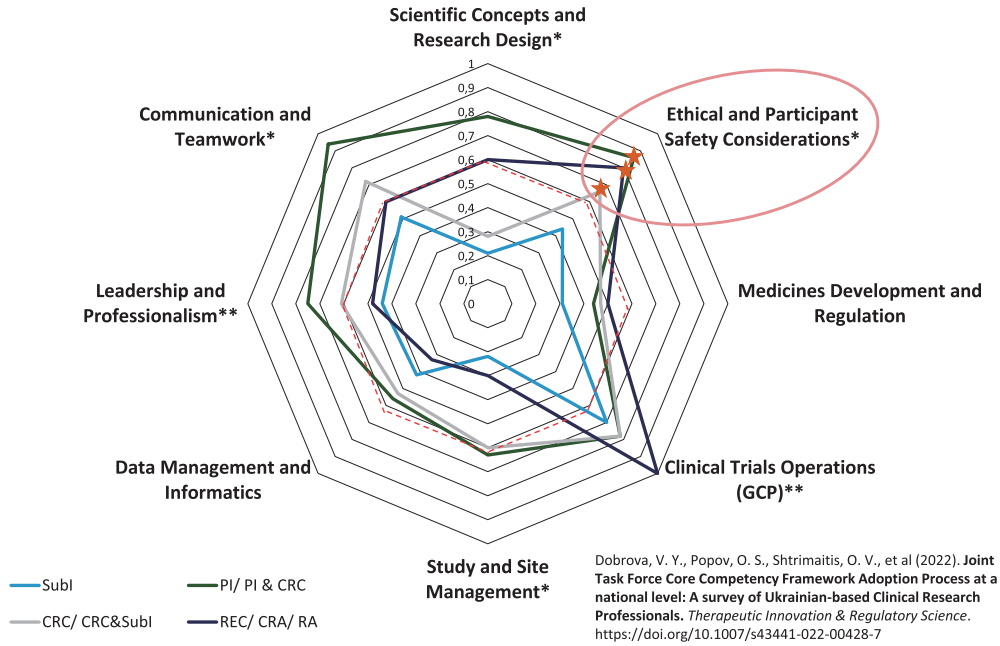
ticipation in REC is voluntary and a non-payment duty for the members. The membership of RECs is completely according to the ICH-GCP norms, a minimum of five people, one of them non-employee, one of them non-research, and a non-medical person. Our RECs have very good support from State Expert Center, and sometimes we have a weak interaction between different RECs, but we have a perfect interaction with State Expert Center. So, each REC can call the special department and ask questions and get help and support from specialists from State Expert Center.

Our research ethics protection system has four capstones. The sponsor is responsible for protection of study subjects. The researcher is responsible for the willingness, well-being, and health of the study subjects. The State Expert Center controls the situation and controls all data of our research. The local REC gets all information about all situations in the trial site and adverse events, different transfers of patients, and many other information. These are the four important capstones for protection of trial subjects.

7. Master's education program

I want to present to you some small research data about our education, because in Ukraine we pay attention not only to how we can get money from sponsors, but we want to conduct clinical trials in our clinical centers at a correspondingly high level of research quality and ensure research subjects (patients) protection (Fig. 4). Long time in Ukraine we had different short-term programs for the training of research personal of clinical trials, clinical associates, monitors, etc. Four years ago, we opened a master educational program "Clinical research", and during this process of opening, my team and I studied a lot of curriculums. We studied curriculum for clinical research professionals, and we did surveys of our researchers, that included our principal

Fig. 4　Self-perceived level of competence in base competence domains by role in clinical trials (Master's educational program "Clinical Research")



Dobrova, V. Y., Popov, O. S., Shtrimaitis, O. V., et al (2022). **Joint Task Force Core Competency Framework Adoption Process at a national level: A survey of Ukrainian-based Clinical Research Professionals.** *Therapeutic Innovation & Regulatory Science*. https://doi.org/10.1007/s43441-022-00428-7

investigators, members of REC, clinical research coordinators, and many other persons who are involved in conducting clinical trials.

You see the data of some assessments of their competency in different questions, and you see that most of them have good competency, more than 60%, according to ethical questions. They want to study these questions and pay attention to get new knowledge and to study it during additional educational programs for clinical research professionals, master's degree educational programs. We designed this curriculum. For us, it is very important to protect first of all our subjects and then get good data and good information for sponsors for future assessment of the efficacy and quality of new medicines and for the healthcare system.

8. Science projects for Ukrainian research ethics system development

The other one that I wanted to show you is that we worked as practical professionals during all this time together with State Expert Center, with Dr. Sergii Rasputniak, together with some of our contract research organizations' members, and together with our friends from different countries: from the United States, from Lithuania, from Latvia. We participated in two big science projects. One is "Identifying and Addressing Challenges of Effective Functioning in the Ukrainian Research Ethics System (2015-2017)". We estimated and assessed how our ethics system worked at that time. As a result of this project, there was an improvement of our State Expert Center and new recommendations, which I showed you before.

The second project "Developing Recommendations for Ethics Committees and Policy Guidance for Eastern European / Central Asian Countries to Support Public Health Emergency Preparedness and Response (2020-2021)" started during COVID-19. I am grateful to Francis Crawley for involving me in this project. We did a good assessment of how our Review Ethics System transformed and worked during COVID time when we saw this pandemic situation, when we get such challenges. This project helped our research community to understand how we can prepare to work online through electronic documents. This project and this time helped us understand how we can work in such a situation in which we are now.

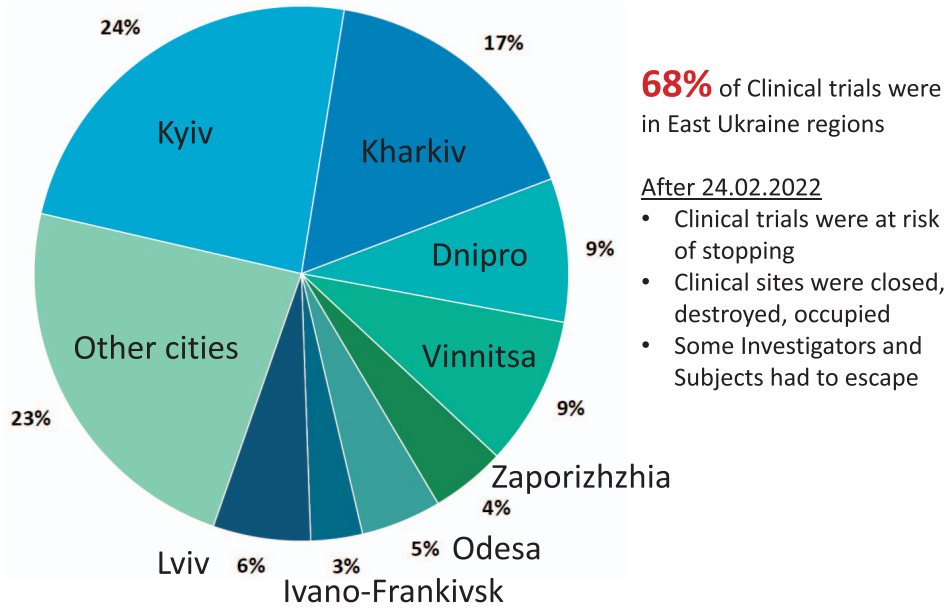
9. Distribution of clinical trials in Ukraine cities

If we come back to our topic of how this war influenced our clinical trial and research ethics system in Ukraine, I want to show you the distribution of clinical trials in Ukrainian sites before the war (Fig. 5). More than 68% of clinical trials were in eastern Ukrainian regions. From the first days, these were the sites that saw Russian aggression, so they needed to take some steps to react to this situation. In fact, after the 24th of February, many clinical trials which were being conducted in these regions were at risk of stopping. Many clinical sites were closed, some were destroyed, and some are occupied even now. Some investigators and subjects had to escape, and our system had to quickly react to this situation and try to come up with the best decision on how to manage such a situation.

10. Transfer of clinical trial subjects

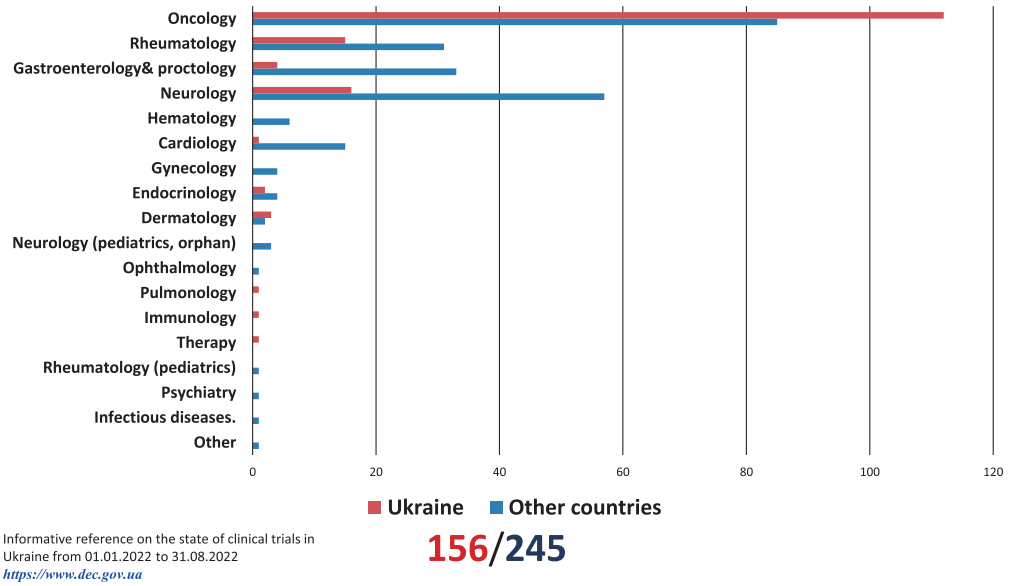
The most important task at this time is how to protect our trial subjects (Fig. 6). First, there was a transfer

Fig. 5　Distribution of clinical trials sites in Ukraine *



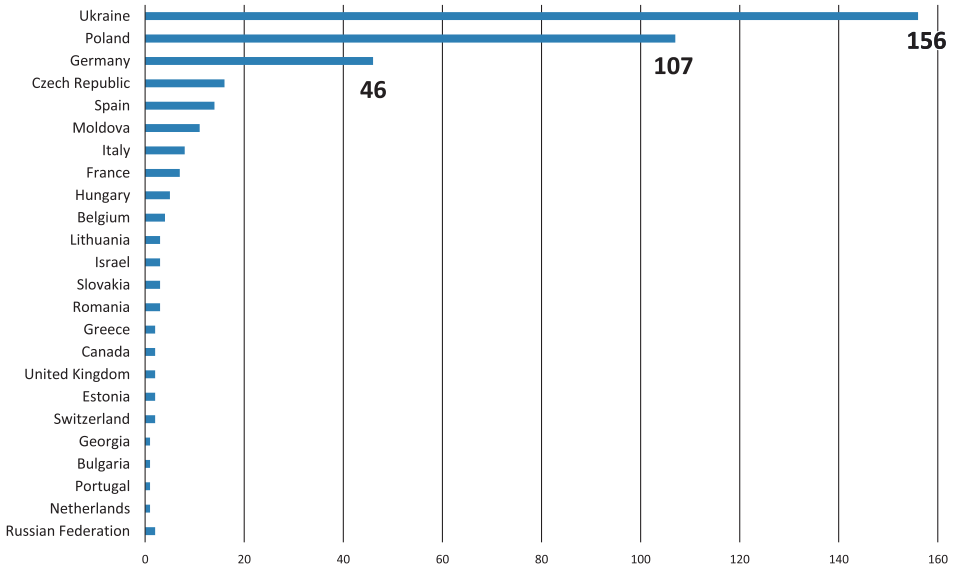
* according to data of State Expert Center Ministry of Health of Ukraine (https://www.dec.gov.ua/materials/aktualna-informacziya/?role=applicant)

Fig. 6　Transfer of clinical trials subjects after 24.02.2022: Nosology



of clinical trial subjects. You can see how this transfer was distributed according to nosology. Most of the oncology patients were moved from the eastern regions of Ukraine as well as to other countries. In fact, neurology, rheumatology, gastroenterology, hematology, and cardiology patients were also moved from the eastern part of Ukraine and to different countries. The number of patients that moved to eastern part of

Fig. 7 Transfer of clinical trials subjects after 24.02.2022: Country



Informative reference on the state of clinical trials in Ukraine from 01.01.2022 to 31.08.2022
https://www.dec.gov.ua

Ukraine is 156 and to other European Union countries is 245.

In terms of the transfer of these patients to different countries, our nearest neighbor, Poland actively started to move these patients to give them an opportunity to continue their participation in clinical trials (Fig. 7). The GCPpl Association in Poland signed new recommendations. They reacted very quickly. Germany also took an active part to move our participants. Some of the participants got an opportunity to participate in clinical trials in German research centers or to prolong their participation in their own clinical trials but in centers in Germany. You see this distribution in other countries like Czech Republic, Spain, Moldova, Italy, France, and others.

11. Clinical trials during the war in Ukraine

When we speak about how in a philosophical or existential way this war influenced our research system and what we need to decide now, all research ethics systems not only of Ukraine but the whole world faced unprecedented challenges by this war. We see clearly what we should do. This is a typical organizational issue experienced by Ukrainian clinical trial research ethics community. This challenge has a lot of uncertainty, complexity, and ethical dilemmas. We clearly see that the assessment of risks and benefits for research subjects should be implemented first. This is that part of the iceberg that we see. We need this instrument of risk-benefit assessment, but what we do not clearly see, and we have some difficulties in clarifying by ourselves but we need to clarify are strategic consequences. How will we feel the long-term impact of this situation of war in Ukraine for all clinical trials system in the world? What strategic ethics consequences and long-time ethical impact should we consider and predict and perhaps prevent them in the future?

12. Issues for research ethics review during war

These are our thoughts about issues of research ethics review during the war (Table 2). The issues experienced by Research Ethics Committee were those related to the process of ethics review and monitoring. First of all, it is a lack of experience. Our members of the RECs, that are working under bombs and missiles, do not have such criteria how to assess the minimal risk for research subjects in these conditions. No one in the world has criteria on how to work and conduct clinical trials in such devastating situations. For example, today, our civilian infrastructures in different cities again were bombed and were under missile attacks by Russian troops. Our RECs do not have criteria for assessment of patients' risk for research procedures and estimations of thier ability to continue such studies.

Another major problem is organizing REC meetings and members' communications. Many members of RECs are employees of these hospitals where clinical trial sites were, and they may be in other countries. They need procedures and need regulations on how to work and how to guarantee assuring transparency and how to do remote work. So, Research Ethics Committee needs to develop procedures that ensure REC member's safety and data confidentiality and conditions of electronic data flow, transparency in conditions of remote work, and compliance with review deadlines. All these tasks are big challenges for volunteer work which research ethics review is.

Table 2　Issues for research ethics review during war: Novel challenges for RECs

- **Protocol review**
  - Risk assessment (study participants)
  - Assuring study personal safety
  - Risk minimization procedures (related to active war)
- **Organization of REC meetings**
  - REC member's safety
  - Data confidentiality (lack of electronic dataflow)
  - Regulation and assuring transparency in conditions of remote work
  - Interaction with others RECs
  - Compliance with review deadlines

Table 3　Issues for research ethics review during war: Ethical monitoring of studies

- Onsite vs remote
  - Risks to safety (REC members, study participants, site personnel)
  - Risks to data confidentiality (paper vs electronic dataflow)
  - Ensuring adequate human subjects protection
  - Impossible to monitor the safety of research subjects in trial sites temporary occupied by Russia
  - Interaction with REC of host clinical trial sites where researched subjects were removed from Ukraine or from some regions of the country

Now, the RECs of Ukraine need to consider special ways for ethical monitoring applying mostly remote methods by constantly evaluating possible risk to the safety for their members, study participants, and ensuring proper human subjects' protection in such a difficult circumstance (Table 3). A very critical question is how to monitor and protect research subjects' rights in this situation when some research subjects are in different countries and

on different site. We need coordination between such sites interchanged by this information. One very difficult and critical question is how to monitor and protect research subject rights on their trial sites that are occupied by Russia and how to manage the interaction between these clinical sites. Taking this into account, it is pretty hard to avoid an excessive burden on Ukrainian RECs, which has not conceded any recommendations. Effective organization of research ethics committee work is still a big question now in Ukraine's research ethics system.

13. Informed consent

Last but not the least is the informed consent problem (Table 4). Some of the potential subjects cannot give consent in the usual way. Some subjects cannot get new information about a change of informed consent. Some of the subjects who were transferred to different countries got informed consent subjects in different languages. How should we organize the translation of these informed consents? How can we organize to support understanding of this informed consent in this situation? In such cases, the witness is obliged to sign and indicate the data on the document, and the researcher must indicate in the primary recommendations how the impartial witness was selected.

Many investigators used calls and remote technologies to obtain consent for the setting and for signing as the first possibility. We do not have clear rules on how to do according to electronic signing, but it is important to mention that investigators were provided these apparently flexible frameworks which were huge barriers for ongoing and new trials. On the other hand, the risk of violation of informed consent quality must be avoided. Therefore, we see a different question, how to work with surrogate informed consent, and how to work with delayed informed consent, how our research ethics committee should assess these types of informed consent. I want to say very trustfully that our Research Ethics Committees do not have a huge experience in working with surrogate informed consent or with delayed informed consent and reviewing of such informed consent. So, it is a very delicate and very important question of how to clarify these topics for our research ethics committee members and also for the clinical trials review system. In this situation, all our investigators try to do it in the best way to avoid additional visits of subjects in clinical sites for the additional signing of informed consent or of data checking. Our investigators do the best way for our patients to protect them to get this data in a remote way, but it is a very big ethical control issue whether it is a good way or not a good way, and the quality of such data is very important and a very big issue for all review systems.

Table 4 Informed consent procedures during war time

- It is necessary to look for alternative procedures to obtain the IC
- The potential subject may give oral consent in the presence of an impartial witness.
- The potential subject and the researcher who responsible for IC process sign and date certain forms of the IC
- Surrogate IC
- Delayed IC
- It is necessary to avoid the supplemental visit of subject to clinical site for IC sign and date

14. Recommendations

I want to say again that from the first day of the active war our state authority and State Expert Center gave recommendations for sponsors on how to work in this situation and some recommendations for ethics committees [1, 2]. If clever and responsible ethics committee member opens sponsor recommendations, they should understand that they are the same participants of the protection of human rights as a sponsor and they are responsible for this protection, so they can use these recommendations for sponsors and can ask for clarifications from State Expert Center on how to work in this situation and use past recommendations and get new recommendations.

Our State Expert Center also gave recommendations for sponsors. They presented it in an open space in their internet site. They clearly recommended using European Union Medicine Agency recommendations (Fig. 8), and they gave a link on their site so everyone can open these recommendations and work according to these recommendations, and conduct reviews according to these recommendations.

Fig. 8　Basic recommendations on the management of clinical trials during active hostilities from the State Expert Center of the Ministry of Health of Ukraine and the EMA (screenshots of web-sites)

1) Recommendations “For sponsors of clinical trials/sponsors’ representatives, investigators, heads of enterprises, institutions and organizations involved in conducting clinical trials” (as of June 1, 2022)

2) Recommendations “For ethics committees, heads of enterprises, institutions and organizations involved in conducting clinical trials”

I would like to draw your attention to these main topics, the responsibility of sponsors for assessing the feasibility of new clinical trials, patient recruitment, provision of the possibility of patient transfer to another trial site in Ukraine or in other countries, measureing and ensuring the provision of investigational medical product - is it possible to do it or not possible (Table 5). Of course, RECs, if they want to do assessments of new protocol or amendments of protocols, can use these recommendations, these algorithms, and optimize their work according to them.

Table 5 Recommendations from State Expert Center

Main topics:

- ❖ Sponsor's responsibility for assessing the feasibility of a new clinical trial; patients' recruitment
- ❖ Provision for the possibility of the patient's transfer to another trial site in Ukraine and/or in other countries
- ❖ Taking all possible measures to ensure the continuous provision of IMPs to patients at the trial site;
- ❖ Reporting all protocol violations related to patient safety and other trial aspects
- ❖ Optimizing the communication process with patients:
  - ▪ Replacement of physical site visits by telephone contacts or video visits (telemedicine methods),
  - ▪ Rescheduling or canceling visits;
  - ▪ Specifying peculiarities of providing patient's informed consent etc.

Table 6 Research ethics review during war

State authority recommendation:

Apply all possible measures to assure continuous REC functioning according to REC's procedures and requirements, consider measures of individual protection of REC members

Adaptation of RECs Procedures:

•SOPs updating and development

- Remote work of REC members
- The use of online applications (training, funding)
- Risk assessment related to war (criteria for study protocols review, a special check-list)
- Assure effective and safe communication between different RECs, including from foreign countries

Optimization of communication process Research Ethics Committee can use, and we recommend to use of such recommendations as the first basic step to do a review in a good way. In this situation when we do not have a lot of resources, when we are under the pressure of bombing, it is very important to get some recommendations. If we have these recommendations, we can start from these and move forward to do new guidelines exactly for ethics committee, but now it is very important to organize our work and use these proper recommendations.

What main questions are taken into account for these national recommendations (Table 6)? We need to urgently adapt our procedures, particularly related to the remote work of REC members, the use of online applications, criteria for study protocols, new special checklist, new SOPs for effective communication, and all these aspects that requires training, support, funding, and communications between RECs not only of Ukraine but also RECs of different countries. It is very important to get such support and to do this communication.

15. Risks of ethical review during war

What are the global risks of ethical review during war (Table 7)? These are risks of acceleration, and risks of inappropriate ethical review that we have in global way. Despite the public health emergency in these

situations and despite these disaster situations, the RECs should keep in mind and be very careful about the huge risk of accelerated or inappropriate ethical review that involves a range of possible problems such as conflict of interest and therapeutic misconception. We want to look after our patients and help them, but sometimes it is very close to therapeutic misconception. The lack of RECs' members training in reviewing such studies doesn't help to do this review in a good way. In this situation, possible pressure on RECs and their decision grows and intensifies, because the potential benefit for society becomes decisive. It is very easy to take a wrong decision due to urgency of consideration, taking in mind only the potential benefits for society, which can prevail under risk for this study subject, not some unknown participant, but exactly for this person.

Table 7　Risks of accelerated/inappropriate ethical review during war

- Conflict of interest
- Therapeutic misconception
- Insufficient level of knowledge and competence of REC member
- Influence of different restrictions on REC work
- Possible pressure of global problems significance on local REC decision
- Errors and imperfections of the process due to the urgency of consideration
- Reassessment of benefits for society
- Insufficient communication with other stakeholders
- Insufficient transparency and public involvement

A very big problem is the low cooperation between different RECs inside Ukraine. When participants move to another site, the RECs from two sides should interact and change information about this participant, but low cooperation between them is still a great problem in Ukraine. Another connected problem is poor communication and insufficient transparency. Today, we do not have a clear roadmap of how to take into account all mentioned issues and how to improve our research ethics system, but we need to think about it and it is very important to make decisions for such issues.

16. Conclusion

Victoria Naumova presented through the face of women the different Ukrainian cities such as Kharkiv, Mariupol completed crushed, Zaporizhia today is under the new bomb attack, Dnipro, Luhansk, Lviv. These cities were the big clinical research centers before 24.02.2022. Why we are speaking about clinical trials not in the Ukraine, not in the past, and why we are thinking about clinical trials in the future? Because all our community, all our society, all our people of Ukraine, are fighting for our future generations, and we think that our future is so bright, and independent that our freedom is very important for us and for all the world because now we are protecting our society, our country. Our people are protecting not only the democracy and choice of Ukraine, but we area also protecting the democracy and choice and independence and liberty of all the world. I believe that in the near future, I can present you information about our new clinical trials, and about rebuilding our research ethics system. I believe that in the near future, we will get this win, and we can present new clinical trials in our country.

As a last note, I want to state the word of Spanish philosopher George Santayana, "Those who do not learn history are doomed to repeat it." So in this situation, it is very important that we learn our history and do our best to not repeat this history again.

Discussion

Q Thank you so much for your brilliant presentation. Every time you present during this war, it gets even better and better. It was so clear. You made it so evident, and you gave us real direction. Could you say like a summary of what you said what should we be doing now?

Dobrova For me, it is a very philosophical question. What we should do now for our research community, we are doing now the very important thing that we discuss this topic for all the world, not only inside Ukraine or not only between Ukrainian people, and we try to find a decision on how to manage it in the best way. For the ethics review system, for clinical trials system, all that we do is very important and this information that we give to people all over the world is very important, but if we speak about how to manage this situation, I want to ask all people involved. I know that many people now say: "We are tired, we have some problems, we are afraid of the nearest winter, we are afraid of the nearest heating season, for example, in Western Europe, we are afraid that our economy will crash, we are afraid that it is not a good way to continue the fight". I want to repeat the words of Joe Bayden: "If Russia stops its invasion, the war will end right now. If Ukrainians stop defending themselves, it will be the end of Ukraine." So, Ukraine cannot stop fighting if the community and the world find the power to support us, not protect us, because we protect ourselves and we fight for our future. Therefore, in a more philosophical way, do not be tired but believe in Ukraine, believe in our army, believe in our people, and you will see we can manage in a good way. We will meet each other in the next year or in the next to next year in Kyiv, at a big conference, similar to what we participated with Francis from State Expert Center. We will discuss how to improve our system, how to drive our system in European Union according to Regulation 536, so believe us and support us.

Q I would like to ask you that under such a stressful situation, would it not it be better to have one national ethics committee in Ukraine? In Hungary, we have one national ethics committee for all the clinical trials in which new non-registered drugs are used.

Dobrova About 15 years ago, we had one central ethics committee, but our Ukrainian law on medicine contains articles according to which the rights and safety of research subjects must be protected by local ethics committees. Therefore, in this situation, to make one ethics committee which will work I do not think is the best way today. Maybe in the future when the war is over, it will be good to find a coordination center as we started to do with Sergii Rasputniak and State Expert Center. In 2018, we started to do this work after our research which founds some challenges and issues within our research ethics system. But now it is not very good, because according to our legislation, the Ukrainian RECs are not a paid organization. For people who are independent, for people who are working at this local place, it is much easy to understand whether this center is good for clinical trials because the local people are able to see inside these clinical trials site and see their own patients. Now, it is much more important to just give them help and to just give them support, and if research ethics committees have questions, they can easily send them to State Expert Center and get qualified help and explanation.