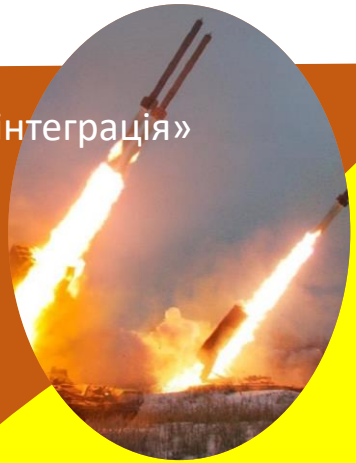
Фармацевтичний форум «Клінічні випробування в Україні. Європейська інтеграція»

Клінічні дослідження в екстремальних умовах. Інновації перевірені війною.



Clinical Trials in Extreme Conditions. Innovations Tested by the War.

Prof. Igor Bondarenko
Head of Oncology and Medical Radiology Department
Dnipro State Medical University, Ukraine

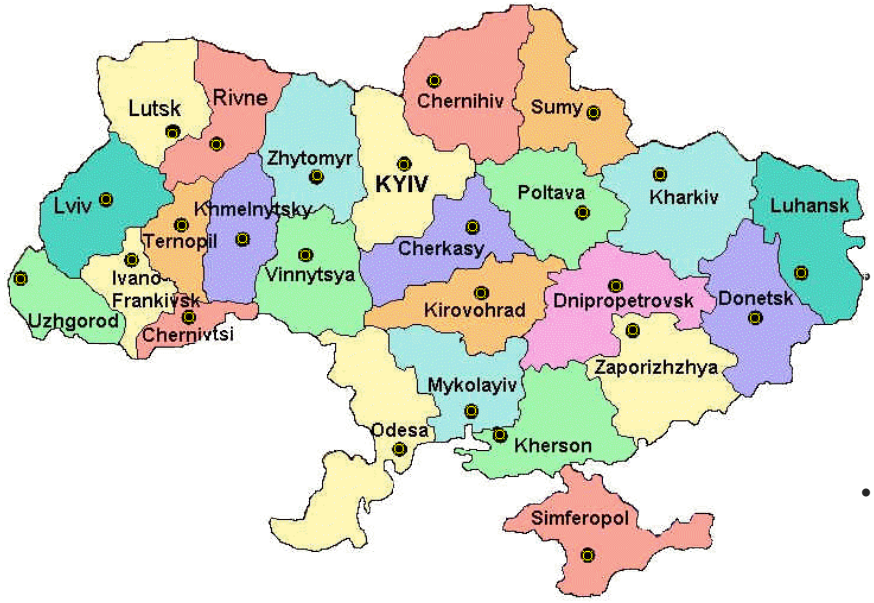
Mercure Kyiv Congress, June 29, 2023

https://www.clinicaltrialsarena.com/clinical-trials-in-extreme-conditions-innovations-tested-by-the-war/?29/06/23/

Before 24 February 2022

Ukraine was perfect place for clinical trials performance

- **About 2500 research sites**
- **Around 500 clinical trials**
- **Approximately 40-50% were oncology trials**



After 24 February 2022

Main aim is to help patients and save the data for Sponsors

- **Majority of sites continues patients' treatment in clinical trials**
- **New patients' randomization is not allowed**
- **No new clinical trials started within the war period**

Ukraine has been receiving unprecedented support from civilized World.
Thank you to all of you!

Previous Publications for the Topic

CLINICAL RESEARCH NEWS
Clinical Trials to the Clinic

In War-Torn Ukraine, Clinical Trials Trudge Along

By Deborah Borfitz

ELSEVIER

Annals of Medicine and Surgery
Volume 80, August 2022, 104271

Correspondence

Healthcare system amidst the war in Ukraine

Anastasiia D. Shkodina, Hitesh Chopra, Inderbir Singh, Shoaib Ahmad, Dmytro I. Boiko

JCO® Global Oncology
An American Society of Clinical Oncology Journal

MENU

JCO Global Oncology > List of Issues > Volume 8 >

REVIEW ARTICLES | Cancer Prevention and Control

The Armed Conflict and the Impact on Patients With Cancer in Ukraine: Urgent Considerations

Christian Caglevic, MD[1,2]; Christian Rolfo, MD, PhD, MBA, Drhc[3]; Ignacio Gil-Bazo, MD, PhD[4]; Andrés Cardona, MD, MSc, PhD, MBA[5]; Jorge Sapunar, MD[1]; Fred R. Hirsch, MD, PhD[6]; ...

frontiers | Frontiers in Medicine

The continuation of clinical trials in times of war: A need to develop ethics and situationally adaptive clinical research guidelines

Chieko Kurihara[1*†], Francis P. Crawley[2†], Varvara Baroutsou[3†], Sander Becker[4†], Brigitte Franke-Bray[5†], Courtney A. Granville[6], Kotone Matsuyama[7†], Shehla Naseem[8†], Johanna Schenk[9†] and

Current State of Clinical Trials Impacted by the War in Ukraine

BY TYLER HOEY, CORTNEY MILLER AND SHAWN ROACH
THU, MAY 12TH 2022

WIRED BACKCHANNEL BUSINESS CULTURE GEAR IDEAS MORE SIGN IN

GRACE BROWNE SCIENCE MAR 14, 2022 7:00 AM

The War Puts Ukraine's Clinical Trials—and Patients—in Jeopardy

Most of the clinical trials will be completed within 2-3 months.

This is a great challenge for hundreds of experienced specialists and thousands of patients.

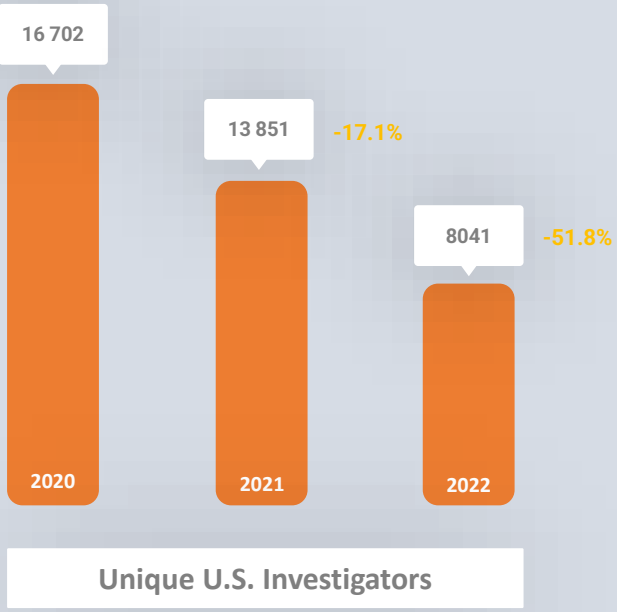
Ukraine has safe locations to conduct new clinical trials.

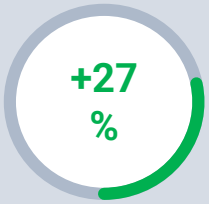
Sponsors Companies of clinical trials – please come back to Ukraine.

This will be the best solidarity reflection with Ukraine!

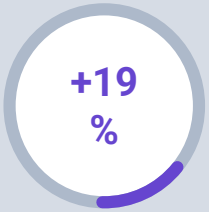
Thank you

Clinical Trials Statistics

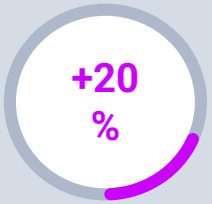




↑ Number of endpoints



↑ Number of trials with 3-4 arms



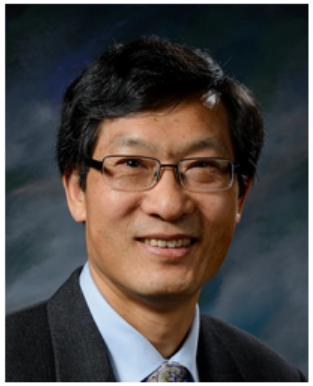
↑ Number of trials with 5 arms

CLINICAL TRIALS BECOME HARDER TO CONDUCT

Phesi Report: Assessing Single Patient Investigator Sites in Cancer Clinical Trials

Published on: January 25, 2023
Gen Li, PhD, MBA

Already existing enrollment challenges emphasized by single patient sites.


Gen Li

Patient enrollment performance is a chronic challenge in clinical development. Three years of the COVID-19 pandemic has caused a number of investigators to back out from participating in clinical trials, and the war in Ukraine has reduced geographic coverage for trials in various indications. Moreover, a global economic downturn and intensifying global inflation have made already costly clinical trials more expensive.

In this report, we leverage site level patient enrollment data in Phesi's Trial Accelerator platform to assess the number of investigator sites that have recruited only one patient, the impact from those sites, and possible methods to improve enrollment.

The dataset

A total of 173 cancer clinical trials with site level enrollment data, the majority conducted in the past three years, are included in this analysis. Most of the trials severely impacted by COVID-19 are not included. Overall, cancer trials take at least three years to complete and publish results; the cancer trials started before or during the pandemic and affected by the shutdown do not yet have available enrollment data. In the dataset, there are 11,826 investigator sites that enrolled one or more patients, totaling 83,916 patients.

Phesi and Tufts CSDD analysis of 173 cancer trials

19%

of all sites

contribute less than 3% of the enrolled patients

11%

of all sites

fail to enroll a single patient

37%

of all sites

under-enroll

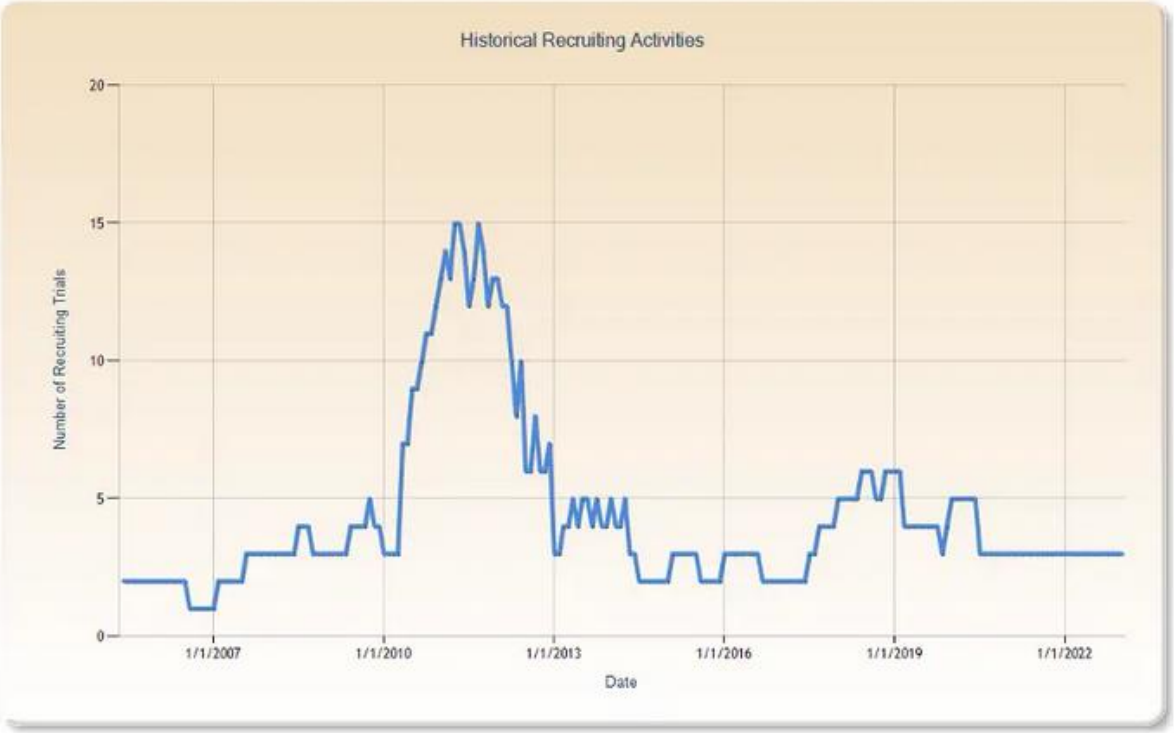
16%

of all sites

contribute 54% of the enrolled patients

Case study: Examples of successful enrollment

Igor Bondarenko, MD, PhD, from Ukraine is one of the most prolific investigators among the 173 trials. He enrolled 113 patients for the 11 trials in which he participated. The median number of patients he enrolled is nine. There is no trial where he enrolled only a single patient.



Is it possible to conduct clinical trials during war?

Workload of Professor Igor Bondarenko site (Dnipro, Ukraine) since 24.02.2022 (martial law period)

- Total number of conducted clinical trials - 44
- Total number of patient's visits - 3987
- Laboratory tests - 3291
- Intravenous infusions – 1800
- IP (tablets) dispensing - 1048
- Injections - 179
- ECG - 831
- CT examinations (tumor assessment) - 1117
- Telephone Follow Up – 861

I AM PROUD OF MY TEAM!

Highly Cited Researchers (329) in Oncology

Country	Number of HCRs
United States	140
France	15
Germany	15
United Kingdom	12
Italy	10
Republic of Korea	10
Australia	8
Spain	6
China	5
Belgium	3

Country	Number of HCRs
Canada	3
Japan	3
Netherlands	3
Switzerland	3
Ukraine	1
Greece	1
Poland	1
Singapore	1
Taiwan	1

Institutions with Highly Cited Researchers in Oncology

Institution	Number of HCRs
Memorial Sloan Kettering Cancer Center, United States	45
UTMD Anderson Cancer Center, United States	22
Dana-Farber Cancer Institute, United States	10
Harvard University, United States	9
Universite Paris Saclay, France	7
American Cancer Society, United States	4
Yale University, United States	3
University of Sydney, Australia	3
University of Milan, Italy	3
Sungkyunkwan University (SKKU), Republic of Korea	3
...	
University of Barcelona, Spain	2
Dnipro State Medical University, Ukraine	1

Institution	Number of HCRs
Institute of Cancer Research - UK, United Kingdom	2
Seoul National University (SNU), Republic of Korea	2
Yonsei University, Republic of Korea	2
Kindai University (Kinki University), Japan	2
Asan Medical Center, Republic of Korea	1
Chungbuk National University, Republic of Korea	1
University of Montreal, Canada	1
Netherlands Cancer Institute, Netherlands	1
University of Zurich, Switzerland	1
National & Kapodistrian University of Athens, Greece	1
Ulsan National Institute of Science & Technology (UNIST), Republic of Korea	1
Nanyang Technological University, Singapore	1
National Taiwan University, Taiwan	1

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Highly Cited Researchers

2022 Recipients | Researcher stories | Analysis | Methodology | Past lists | FAQs

Award category | Institution | Ukraine

Search by name | Submit

FULL NAME	CATEGORY	PRIMARY AFFILIATION	SECONDARY AFFILIATIONS	
IB Bondarenko, Igor M.	Clinical Medicine	Dnipropetrovsk State Medical Academy, Ukraine		View Profile

Clinical Trials Challenges During War in Ukraine

Human Resources

1. **Patients relocation** makes further participation in trial less possible
2. **Site's staff relocation** causes the lack of experienced investigators and coordinators
3. Inability to perform clinical trial **activity in sites close to battle fields**

Data Resources

1. Logistic issues causes **delayed in sample handling** and sites supply
2. CRO and sites have to adapt quick solutions to **enable remote monitoring**
3. High **risk of data loss** due to air attacks

New Paradigm
for future clinical trial process

- Fast
- Less Expensive
- More Accurate
- Motivate Site
- Remote Technologies

Assist

Sponsor creates protocol
and
Site Assistant System
for all sites around the world

Create

One **super template**
for specific clinical trial
for all involved sites

Interact

Multi-lingual system
provides easy communication

eurizon
European network
for developing new horizons for RIs

2.2 Research project description template

EURIZON FELLOWSHIP PROGRAMME

"Remote Research Grants"

Valid applications need to be submitted through the website: https://indico.desy.de/event/38700/ by the Principal Investigator of the Ukrainian team before May 8th 2023 at 12:00 Pm (noon) CEST time. Before applying please read carefully the Terms of Reference (ToR).

Title[1] of the research project: *(max 30 words)*
Developing a new paradigm for conducting oncology clinical trials during emergencies

submitted by

PRINCIPAL INVESTIGATOR (PI)[2]:

First name and Family name (English)	*Igor Bondarenko*

What should be done?

Step 01

Investigate research site problems

Step 02

Learn the experience of successful site

Step 03

Implement appropriate software solutions

Step 04

Share applied principles with others

SITE ACTIVITIES' PROBLEMS

1. Quality of data and timing in complex trials
2. Safe drug storage and accountability
3. No on-site monitoring
4. Accuracy and timing of payments
5. Fast and quality communication

SITE SOLUTIONS – NEW SOFTWARE

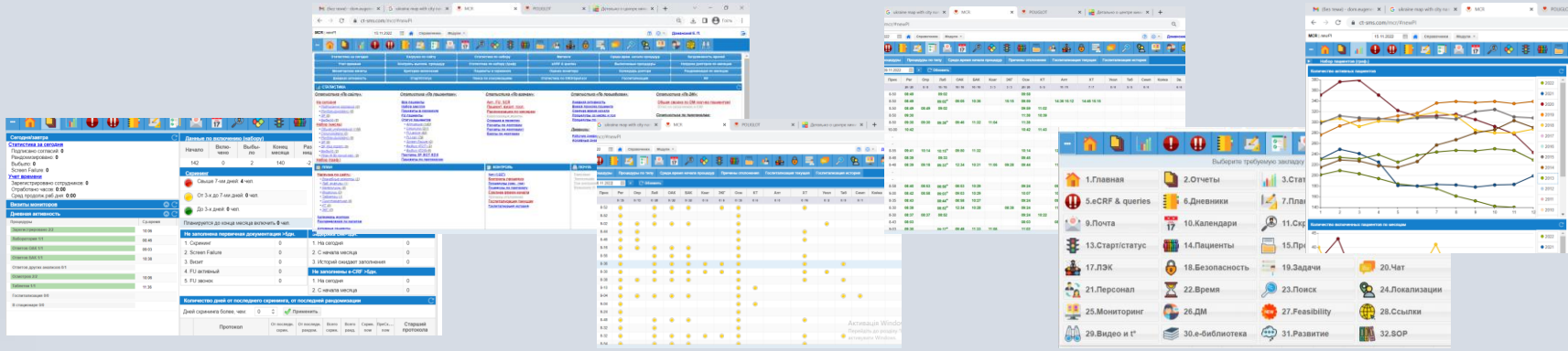
Clinical Trials Site Management System (CTSMS) - MCR

1. Site Support System
   Prevent mistakes, stick to the protocol
2. Pharmacy management tool
   Help to avoid drug insufficiency
3. Software for remote monitoring
   Secure, comfortable, 24/7 (365)
4. Automated system for precise invoicing
   Accurate, fast, without errors
5. Multilingual automatic translation system – Polyglot ™
   Available at least 17 languages

CTSMS

Clinical Trials Site Management System

one step ahead to open the future of clinical trials



COMPETITION

MCR

Focused on

Site Activities

+

Sponsor Activities

and

CRO Activities

Focused on

Sponsor Activities

and

CRO Activities

ADVARRA

CLOUDBYZ

edge

trialkit

Jeeva INFORMATICS

REALTIME CLINICAL TRIAL MANAGEMENT SYSTEMS

OpenClinica

COMPETITION

MCR

Site Activities

- ✓ Site departments workflow
- ✓ Each department has it own dashboard
- ✓ In-depth planning
- ✓ Procedures' execution control
- ✓ Medical documents creation
- ✓ Drug storage and accountability
- ✓ Complete principal investigator awareness
- ✓ Possibility to auto complete EDC from CTSMS
- ✓ Remote monitoring
- ✓ Trials procedures tracking and invoicing
- ✓ LEC/IRB communication tool
- ✓ All solutions in one system

Sponsor/ CRO Activities

- General planning
- Data capture solutions
- Overall statistics
- Budgeting

ADVARRA

CLOUDBYZ

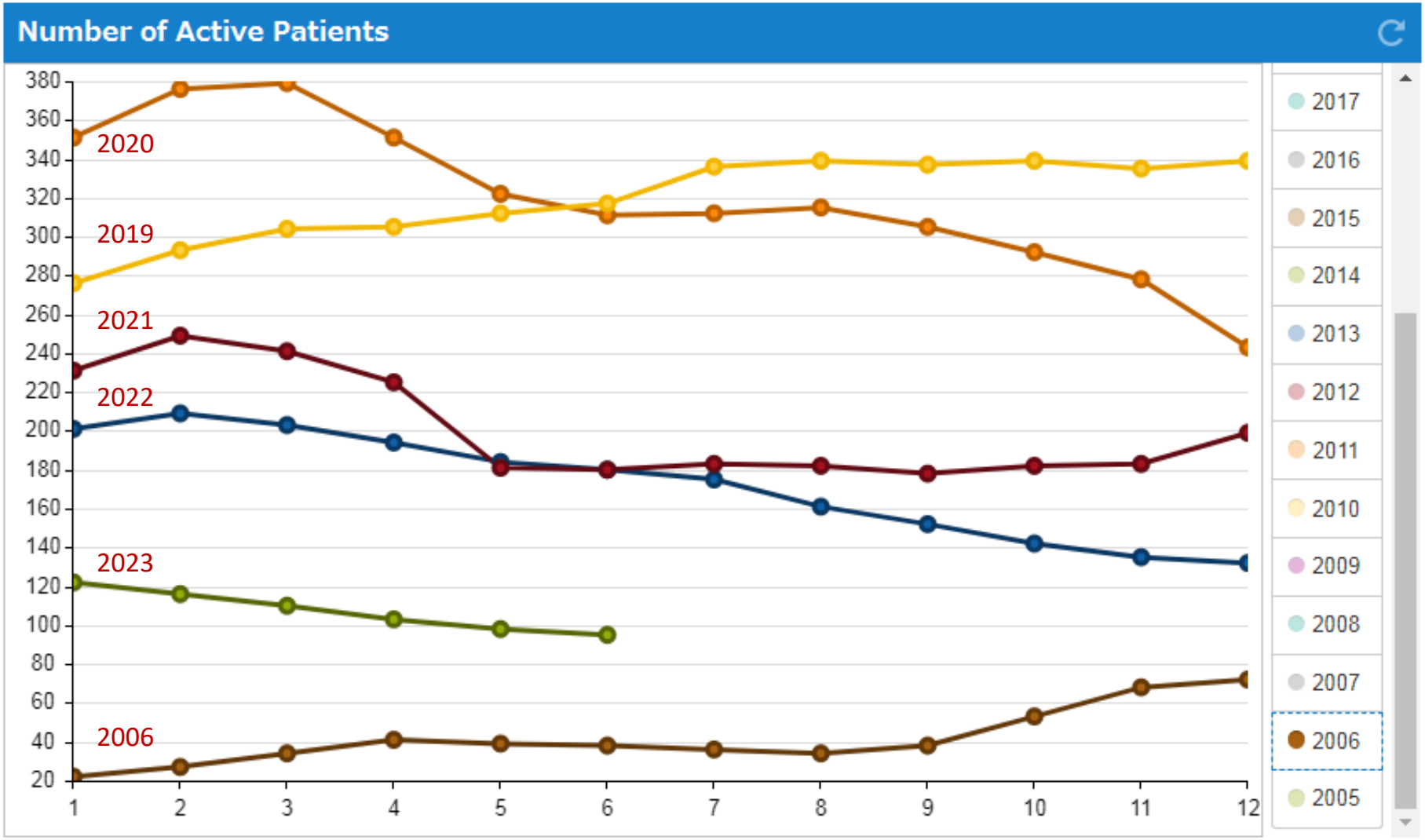
edge

trialkit

Jeeva INFORMATICS

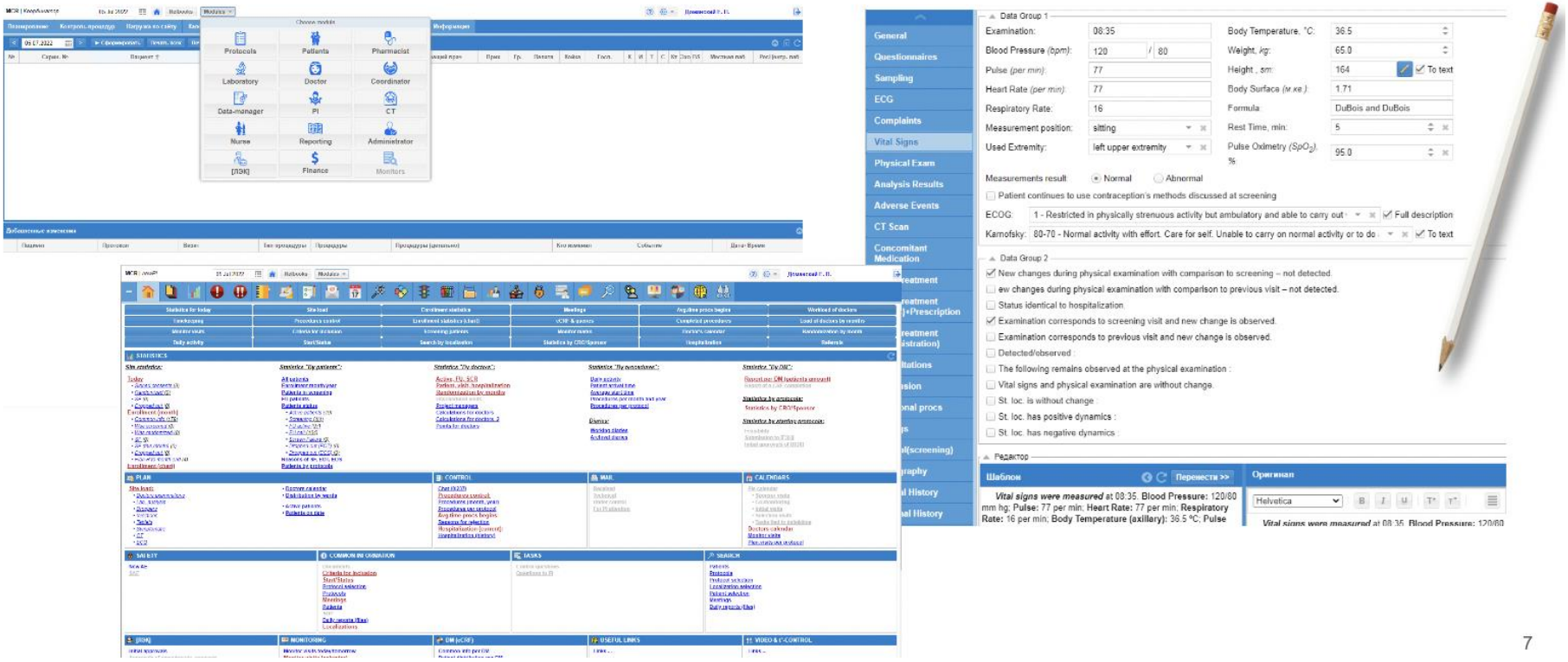
REALTIME CLINICAL TRIAL MANAGEMENT SYSTEMS

OpenClinica

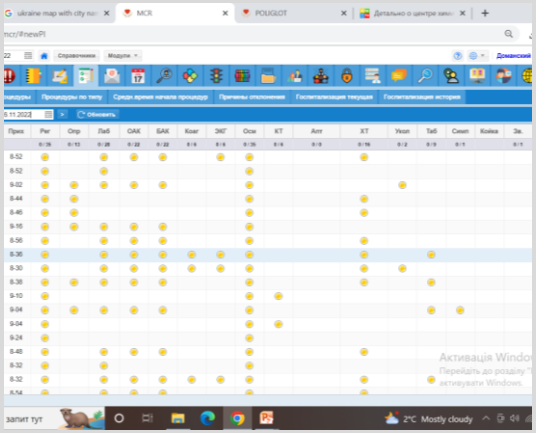

Number of Active Patients
2020
2019
2021
2022
2023
2006
2017
2016
2015
2014
2013
2012
2011
2010
2009
2008
2007
2006
2005

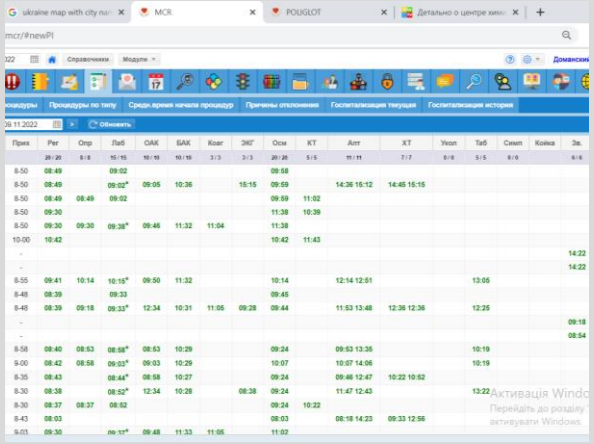
MCR - Smart clinical trials site management Platform

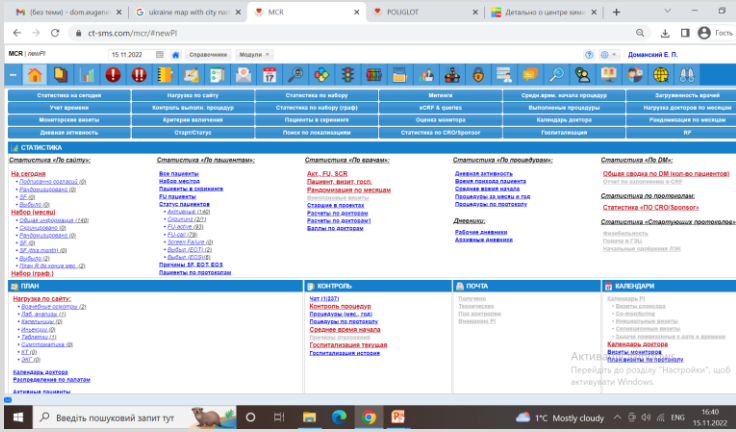
aimed to coordinate and arrange all activities from site selection through trial conduction to authorities' inspection

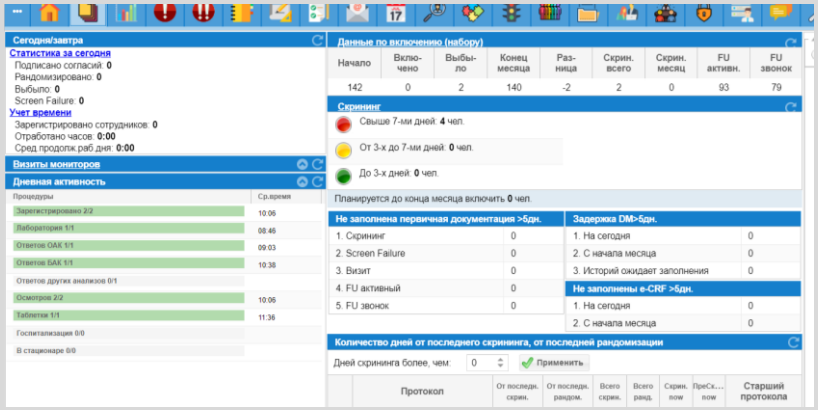


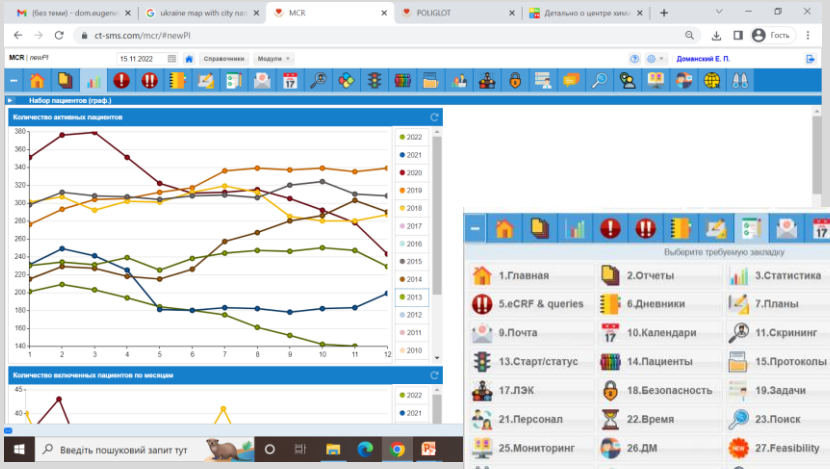
CTSMS – MCR (Medical Clinical Research)











Poliglot

		Abbr	Language		Text
1	☐	en	English		Thank you all for your attention! We wish peace and prosperity!
2	☐	uk	Ukrainian		Дякуємо всім за увагу! Бажаємо миру та процвітання!
3	☐	ru	Russian		Благодарим всех за внимание ! Желаем мира и процветания !
4	☐	de	Deutsch		Vielen Dank für Ihre Aufmerksamkeit! Wir wünschen Frieden und Wohlstand!
5	☐	pl	Polish		Dziękuję wszystkim za uwagę! Życzymy pokoju i pomyślności!
6	☐	it	Italian		Grazie a tutti per l'attenzione! Auguriamo pace e prosperità!
7	☐	es	Spanish		¡Gracias a todos por su atención! ¡Deseamos paz y prosperidad!
8	☐	fr	French		Merci à tous pour votre attention ! Nous souhaitons la paix et la prospérité!
9	☐	nl	Nederlands		Dank u allemaal voor uw aandacht! Wij wensen vrede en voorspoed!
10	☐	pt	Portuguese		Obrigado a todos pela atenção! Desejamos paz e prosperidade!
11	☐	cs	Czech		Děkuji všem za pozornost! Přejeme mír a prosperitu!
12	☐	tr	Turkish		İlginiz için hepinize teşekkür ederim! Barış ve refah diliyoruz!
13	☐	he	Hebrew		תודה לכולכם על תשומת הלב! אנו מאחלים שלום ושגשוג!
14	☐	zh	Chinese		谢谢大家的关注！我们祝和平与繁荣！
15	☐	ar	Arabic		شكرا لكم جميعا على اهتمامكم! نتمنى السلام والازدهار!
16	☐	ja	Japanese		ご清聴ありがとうございました！私たちは平和と繁栄を願っています！
17	☐	ko	Korean		관심을 가져 주셔서 감사합니다! 우리는 평화와 번영을 기원합니다!

Available Site Solutions

- eConsent
- ePRO/eCOA
- eSource
- eSiteFile
- Telehealth
- Recruitment portals
- Remote monitoring

cover **SOME** processes around research site and **NO** processes wihtin the site

Site Crucial Processes

- Site Departments' Activities Planning
- Tracking and Controlling of all ongoing Processes
- Coordinating Site's Team and Units
- Source Recording of Protocol Specific Data
- Financial Tracking and Motivation

Essential MCR Services

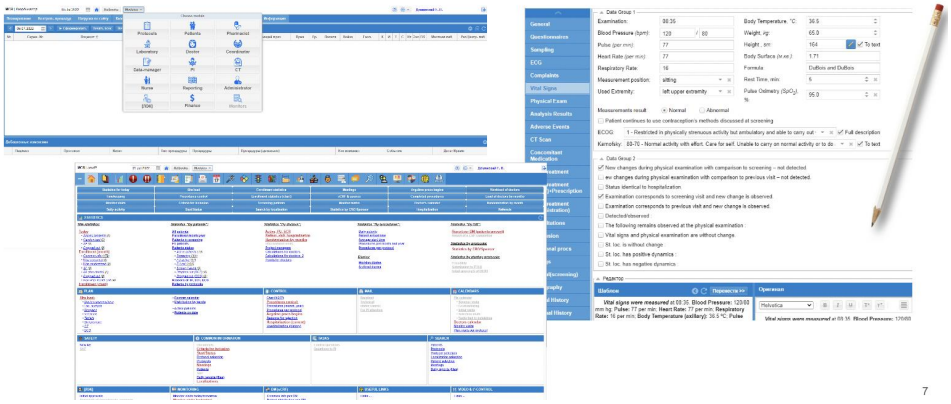
01
Deep planning
Full protocol and site activities scheduling

02
All activities control
Supervise each step in trial conduction

03
Create medical documentation
Quality and accuracy of data

MCR - Smart clinical trials site management Platform

aimed to coordinate and arrange all activities from site selection through trial conduction to authorities' inspection



04
Remote mode of work
Remote Data-management and monitoring

05
Automated invoicing
100% automated payments managements

06
Multilanguage usage
User interface and documents creation in at least 17 languages

MCR COVERS THE WORK OF ALL DEPARTMENTS

- Protocol
- Patient
- Pharmacy
- Laboratory
- Doctor
- Coordinator
- Data-management
- PI
- CT
- Nurse
- Report
- Administrator
- LEC / IRB
- Finance
- CRA

MIS – Medical Information Systems

DEEP PLANNING

Use study schedule

Adjust site routine activities

Inform internal departments

Form the base for all time points

150 Key Questions for Site Initiation Visit

Analysis deep planning example

21 parameters are required to plan one analysis

Analysis parameters (EOT > Q2 Solution (QL) > Blood for Plasma Biomarker Analyses)

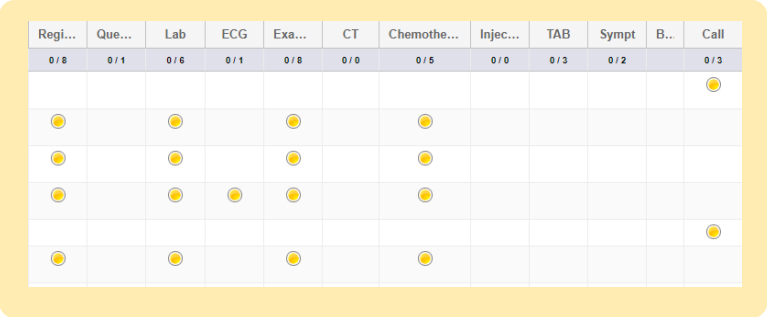
Parameter	Value
Analysis name	Blood for Plasma Biomarker Analyses
Ambient/frozen	Ambient
Component	Plasma
Uphold	No
Uphold, min	0
Centrifuge process	No
Centrifuge process, min.	0
Cold centrifuge	No
Centrifuge speed. rot/min	0
Centrifuge turn	0
Storage temperature	0

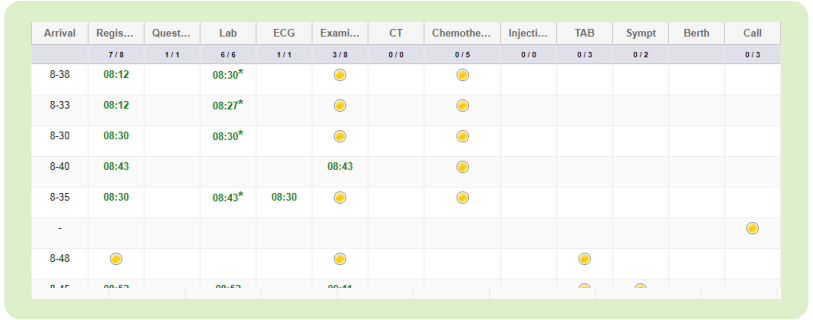
Test tubes

Name		Amount	t,°C	Courier	Send in , days	Pre-/ post dose	Drug	Starting point	Time			
Lab kit	Tube/ slide								From		to	
									t...	m..	t...	m..

ACTIVITIES CONTROL

All planned activities appear on the day schedule.
Once the procedure is marked as done, the time of completions will be saved





- Patient registration
- Questionnaires completion
- Analysis collection
- Analysis results
- ECG
- Examination
- Study drug dispensing
- Study drug infusion
- Injection
- Oral drug administration
- Symptomatic treatment
- CT
- Bad occupied
- FU phone call

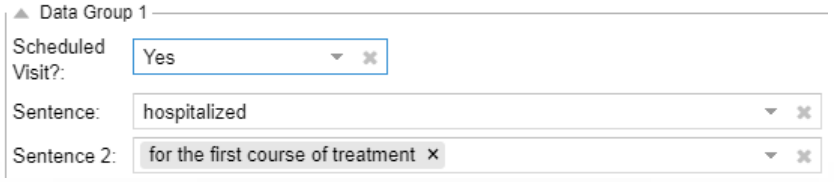
Critical time-points are registered, used for performance analysis and study activities management

MEDICAL RECORDS CREATION

- General
- Questionnaires
- Sampling
- ECG
- Complaints
- Vital Signs
- Physical Examination
- Analysis Results
- Adverse Events
- CT
- Concomitant Medication
- Study Treatment
- Consultations
- Conclusion

Patient record is divided according to standard procedures and each section is placed chronologically based on sequence order

Select data from drop-down menu
or
Enter data manually



and

site assistant will create the sentence

Patient was hospitalized for the first cycles of treatment within the scheduled time frame

TEMPLATING

Study Protocol

Lorem ipsum dolor sit amet. Sed sequi nostrum hic cupiditate voluptatem qui amet magnam qui minus internos quo doloremque provident. Ex quibusdam libero est quos omnis qui voluptate dignissimos ea voluptatem cupiditate ea quidem minus et deleniti distinctio et alias assumenda.

PK postdose must be collected at the end of IP infusion, 2 and 4 hours after the end of IP infusion.

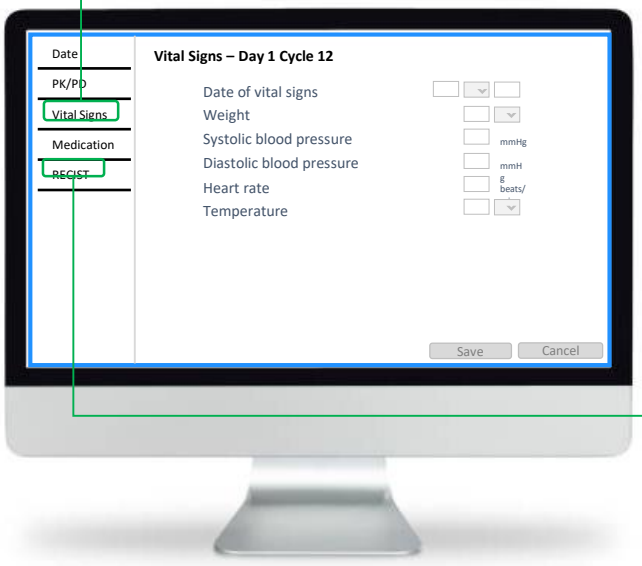
Ut velit beatae non cumque repellendus qui maiores iure est magni aperiam. Cum perferendis nihil vel consequatur dolorum ea dignissimos consequatur. Et excepturi perferendis aut soluta debitis sed deleniti eveniet eum blanditiis aspernatur eum dolores eius et obcaecati enim. Ut quibusdam iste eos officia doloremque et aliquid molestias.

Any protocol-specific data can be added to medical record template for a particular study and doctor will never forget to evaluate such data

Action order *(Template: M)*

	Drug	Form	Prompt	Text
7	M	Text	Введення препарату виконувалося в праву/ліву ліктьову вену.	Введення препарату виконувалося в **праву/ ліву** ліктьову вену.
8	M	Summary of input		
9	M	Patient data	в кінці інфузії (EOI) (± 10 хвилин)	
10	M	/Postdose	End of M infusion (+ 10 min)	
11	M	Patient data	через 1 годину (± 10 хвилин) після завершення інфузії.	
12	M	/Postdose	2 hours after end of M infusion (± 10 min)	
13	M	Patient data	через 3 години (± 10 хвилин) після завершення інфузії.	
14	M	/Postdose	4 hours after end of M infusion ± 10 min	

EDC/eCRF DATA



Пацієнт планово прибув до клініки для візиту спостереження.
Загальний стан пацієнта задовільний, без негативної динаміки з попереднього візиту.

У 08:20 пацієнт здав аналіз крові у центральну лабораторія (Q2Solution)

Скарги.
Нових скарг не пред'являє. Попередні скарги зберігаються без динаміки.

Об'єктивно о 08:40 **АТ:** 126/73 мм рт. ст.; **Пульс:** 65 /хв.; **Чсс:** 65 /хв.; **ЧД:** 16 /хв.; **Температура тіла (аксилярно):** 36.3 °С.
Вимірювання вітальних функцій проведені в положенні хворого сидячи, після 5 хв. відпочинку.
Вага : 78.5 кг.; **Площа тіла (за формулою Мостеллер) =** 1.97 м².

ECOG - 1 бал.

Нових змін при огляді в порівнянні з попереднім візитом - не виявлено.
При огляді зберігається : зниження маси тіла на 10%, в порівнянні з скринінгом (CS).
St. loc. без змін: без динамики.

Негативні явища

- **сниження ваги 2 ст.** СТС з 26.10.2021, не вирішилось.

Серйозних негативних явищ немає.

Супутня терапія- не приймає

КТ
Пацієнту виконано планову СКТ: *ОГК без контрастування*.
Висновок від радіолога на даний момент не отриманий.

За технічних причин, виконати МРТ ОЧП та ОМТ не можливо. Пацієнт записан на дослідження 06.10.2022.

Висновок:
З пацієнтом проведена бесіда, що при появі нових скарг, погіршенні самопочуття - своєчасно інформувати лікаря-дослідника.
Рекомендовано спостереження онколога, сімейного лікаря за м/проживання.
Продовжувати прийом раніше призначеної супутньої терапії, згідно з рекомендаціями.
Дата наступного візиту: 06.10.2022 / МРТ ОЧП та ОМТ
Пацієнт в задовільному стані відпущений додому самостійно.

Identify data you need in EDC/eCRF and MCR will highlight it in source and/or transfer it

REMOTE WORKFLOW

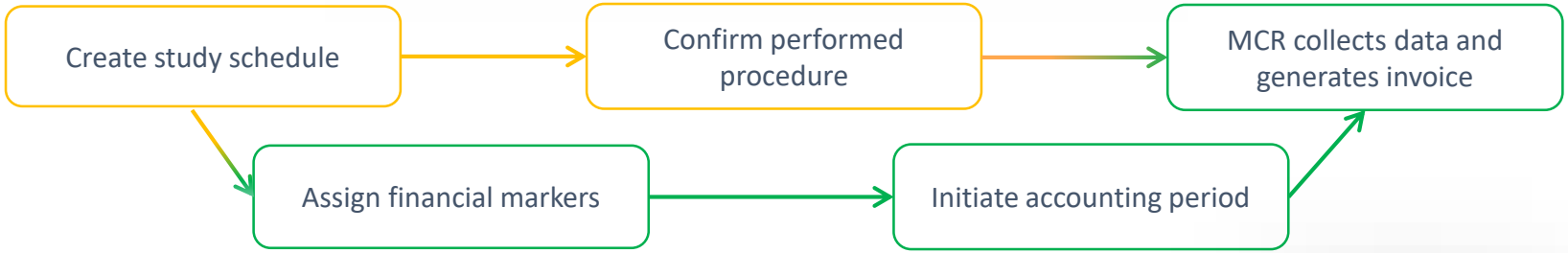
MCR

Secure Server

- Remote data entry
- Remote monitoring
- Remote audits and inspections

Any data collected on site, including paper source documents, is transformed into certified copy, which allows 100% remote activities with such data

AUTOMATED INVOICING



- Financial marker can be assign to a study group, visit, procedures or event
- Each financial marker has a corresponding reference to agreement
- All invoices are divided by initiated by sponsor or initiated by site
- Any clinical trial has its own invoicing schedule

INVOICE

- ✓ Planned
- ✓ Unplanned
- ✓ Additional
- ✓ Study procedures
- ✓ Site Activities
- ✓ Any data

Real Data From Site

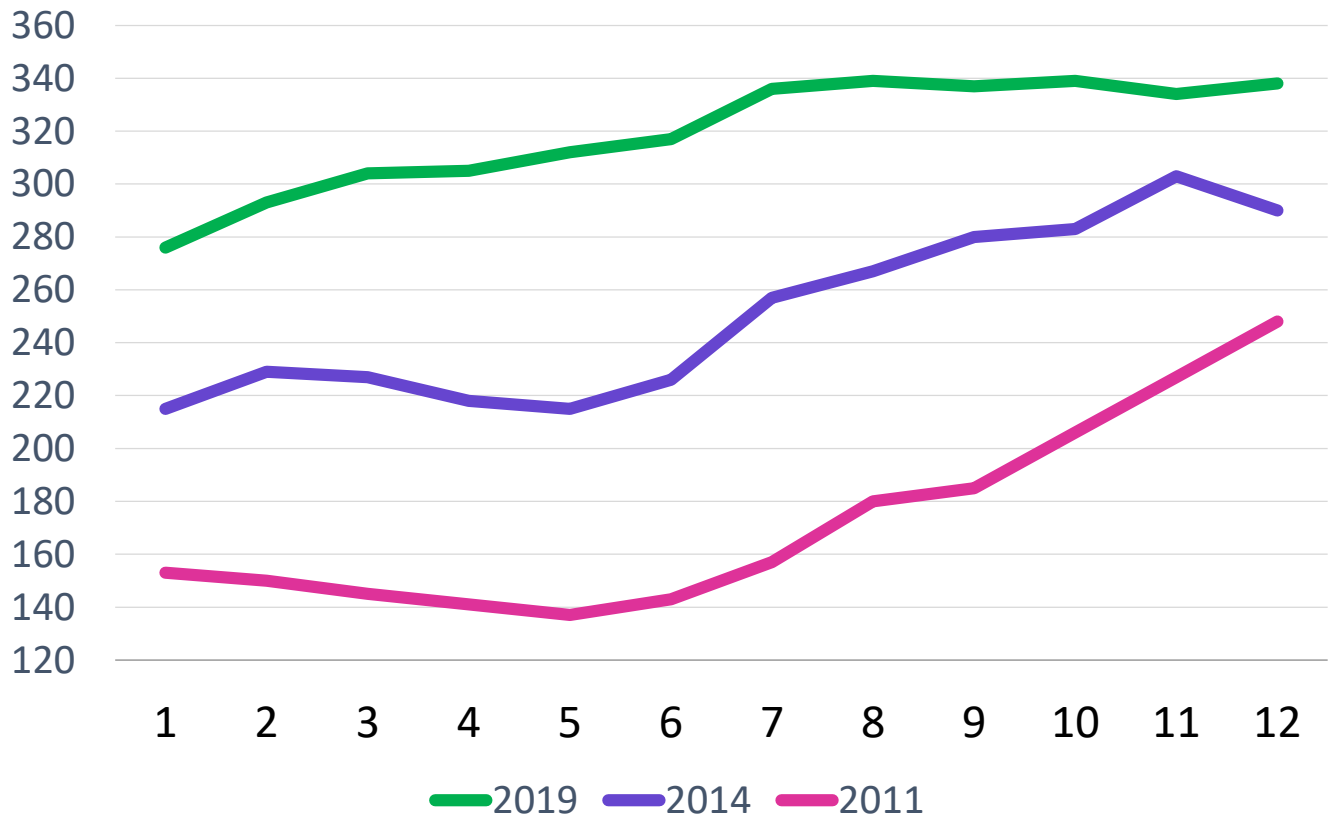
ACTIVE PATIENTS PER MONTH/YEAR CHART

2011 – «Deep Planning» tool was implemented

2014 – «Medical Records Creation» tool was implemented

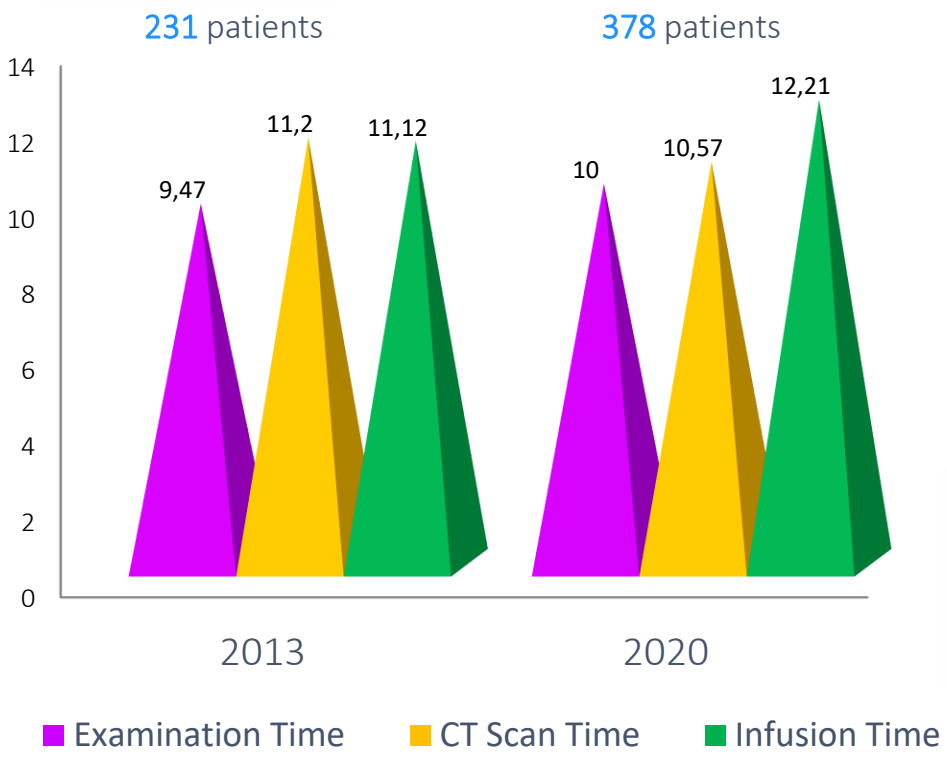
2019 – Starting to analyze statistical data from MCR

Every implemented module of MCR significantly improves productivity and integrity of a research site



Real Data From Site

PROCEDURE AVERAGE START TIME PER DAY

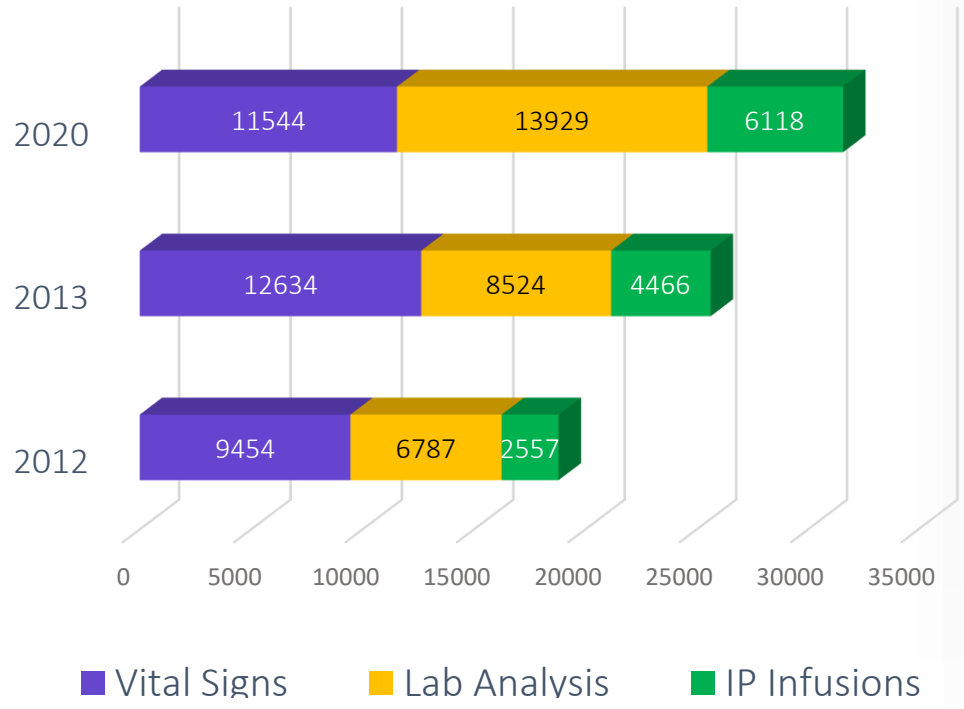


Only well-measured, thought-through planning and coordination with MCR tools helps us to perform more procedures per day within the same number of resources

Physicians	Nurses	Patient beds
18	4	36

Real Data From Site

NUMBER OR PROCEDURES DONE PER YEAR



MCR helps to sophisticate advancements and increase departments' workflow.

Since 2012 MCR is actively used at our testing research site and shows amazing progress.

KNOWLEDGE CENTER

- Videos & Presentations
- Manuals & Handouts
- Live Meeting & Conferences
- On-line chats with Specialists

Watch

Attend

Read

Ask

TOPICS

- ✓ Feasibility
- ✓ Selection
- ✓ Sponsor collaboration
- ✓ IRB/LEC
- ✓ Contracting
- ✓ Study start up preparation
- ✓ Study Initiation
- ✓ First Patient
- ✓ Treatment
- ✓ Completing medical charts
- ✓ Site Departments involvement
- ✓ Working with sponsor tools
- ✓ Monitoring
- ✓ Correspondence
- ✓ EOT and FU activities
- ✓ Invoicing
- ✓ Close out
- ✓ Archiving
- ✓ Audits and inspections
- ✓ Publications

and more...

Who needs knowledge center?

Sites

Regardless of experience

Sponsors

Intending to increase site productivity

Beginners

Who knows little or nothing about trials

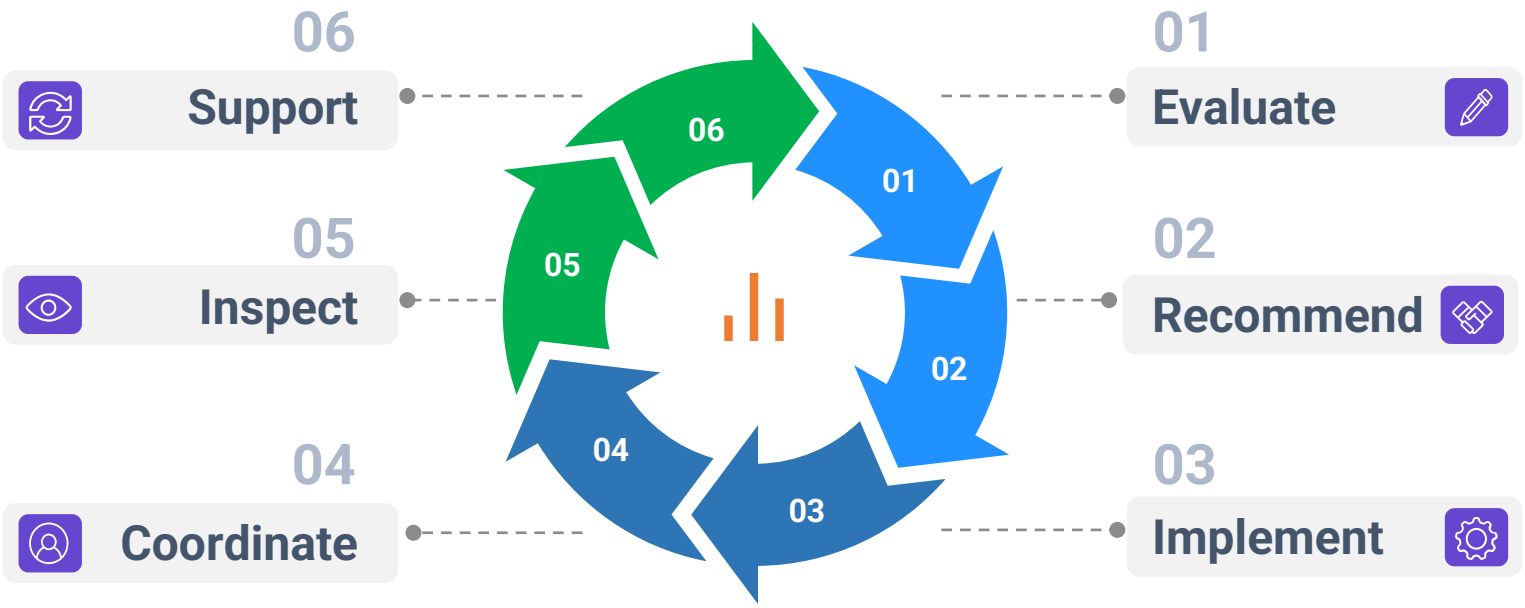
Everyone

Who wants to join the community

MENTOR SERVICE

- Evaluation team
- Coordination team
- Support team

Mentor Service Workflow

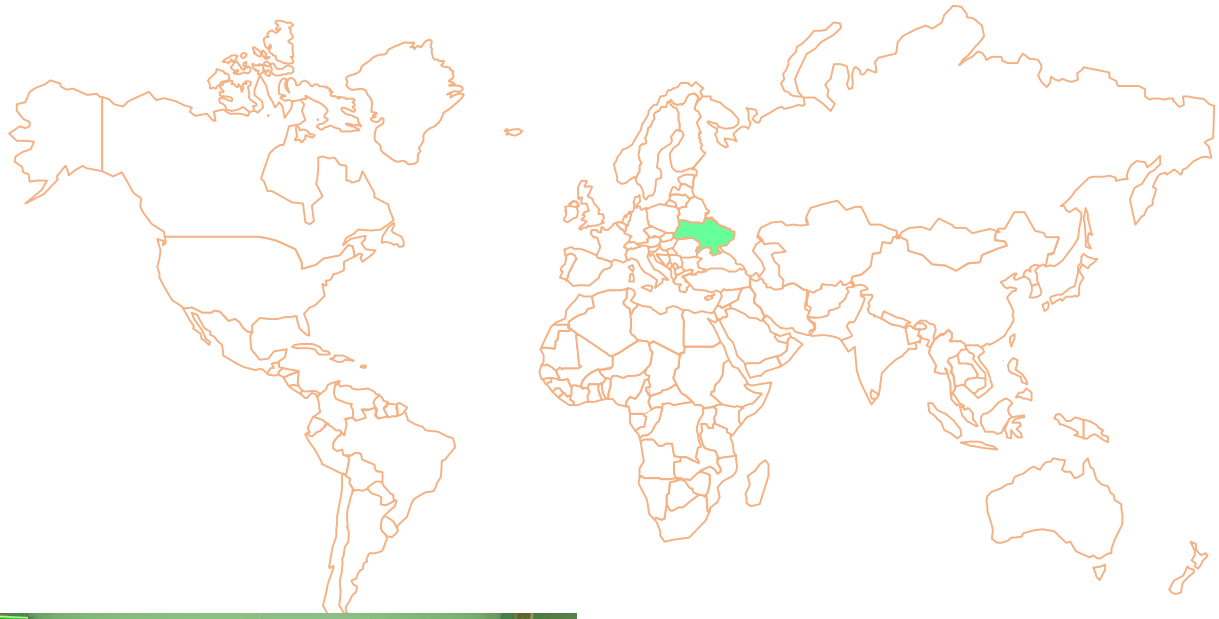


How can we cooperate?

- Learn your mode of work
- Present our mode of work
- Mutual development implementation
- Promote new paradigm of clinical trial conduction
- Grant support of CTSMS MCR

Gratitude to our partners all around the world !

OUR ACHIEVEMENTS SINCE 2002



Dnipro State Medical University,

City Clinical Hospital #4,

Dnipro, Ukraine

4980
TREATED PATIENTS

520
CLINICAL TRIALS

31
TOP ENROLLMENT

150
AUDITS

3
FDA INSPECTIONS

430
PUBLICATIONS

Ukraine is thankful to the whole world for the help and support

We want to contribute clinical trials

Now it is our time to share our knowledge and provide our solutions for current clinical trial related issues

Let innovate together
Please join us!

Professor Igor Bondarenko

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