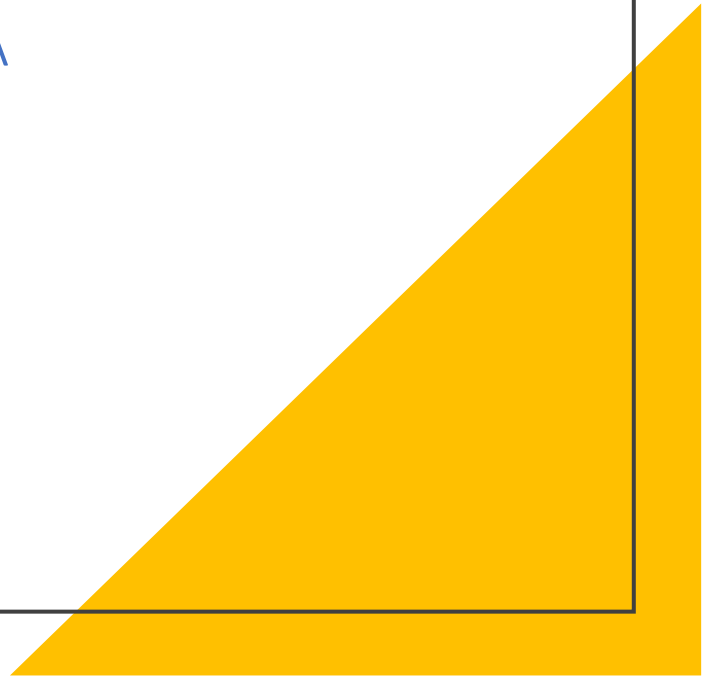


- CREATION OPERATIONAL AND DEVELOPMENT OF THE NATIONAL CENTER OF COMPETENCE IN THE FIELD OF CANCER

CRISTINA BERTEANU

MEDICAL DIRECTOR MEMORIAL ROMANIA

MD;PHD PROJECT DIRECTOR



NCC IS BASED ON A CONSORTIUM OF PUBLIC AND PRIVATE ENTITIES ACCORDING TO ROMANIAN'S NATIONAL RECOVERY AND RESILIENCE PLAN (PNRR), PYLON III SECTION 15.

- DEVELOPMENT OF NCCC IS BASED ON THE IMPLEMENTATION OF RDI PROJECTS WHOSE OBJECTIVES ARE INTERCONNECTED BETWEEN PRIVATE AND PUBLIC PARTNERS, WITH INTERDISCIPLINARY FIELDS, SO THAT THE MAIN GOAL OF THIS CONSORTIUM IS TO BE ACHIEVED

NCCC IS FOCUSED ON IMPROVING THE MANAGEMENT OF  
CANCER PTS BY DEVELOPING INTEGRATED PROGRAMS  
BASED ON THE RECENT ADVANCED IN PERSONALIZED  
MEDICINE TELEMEDICINE , MOLECULAR TUMOR  
CHARACTERIZATION ,IMAGING SYSTEMS AND AI



THE FIVE PARTNERS OF THIS COMPLEX RDI PROJECT HAVE A GEOGRAPHICAL DISTRIBUTION THAT COVERS 3 MAJOR ADMINISTRATIVE DIVISIONS OF ROMANIA

- NORD – VEST DEVELOPMENT REGION
- THE ONCOLOGY INSTITUTE CLUJ-NAPOCA
- NORD-VEST DEVELOPMENT REGION-GRIGORE T.POPA UNIVERSITY OF MEDICINE AND PHARMACY IASI
- BUCURESTI – ILFOV DEVELOPMENT REGION CAROL DAVILA UMFC

P3-POLYTECHNIC UNIVERSITY OF BUCHAREST(UPB)

P5-VICTOR BABES INSTITUTE(IVB)

PARTNERSHIP WITH PRIVATE MEDICAL AND IT COMPANIES FOR DEVELOPED  
STATE OF THE ART DIGITIZED MEDICAL SERVICES




THE SPECIFIC OBJECTIVES OF THIS COMPLEX PROJECT ARE:

1.THE CREATION OF A NATIONAL NETWORK OF CENTERS (NATIONAL NETWORK) INVOLVED IN THE MANAGEMENT OF THE ONCOLOGICAL PETIENT , WITH BOTH ROUTINE ECONOMIC ACTIVITY (MEDICAL ACTIVITY ) AND RESEARCH DEVELOPMENT AND INNOVATON ACTIVITY

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- THE AIM OF THE STUDY IS TO ALLOW COLLABORATION AND ACCESS TO THE WEALTH OF KNOWLEDGE DEVELOPED BY THE NCCC TO ALL PARTNERS AND COLLABORATORS THAT ARE INVOLVED IN SCREENING , DIAGNOSIS AND TREATMENT OF CANCER PATIENTS



2. BUILDING INSTITUTIONAL CAPACITY TO IMPROVE THE COLLECTION OF QUALITY CANCER IN A DIGITIZED NETWORK OF THE REGIONAL CANCER REGISTRIES FOR BETTER ADMINISTRATION IN ONCOLOGY HEALTHCARE AND PUBLIC HEALTH STRATEGY

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BY DEVELOPING THIS APPROACH NCCC WILL DEVELOP AND IMPLEMENT REGIONAL /NATIONAL CLINICAL TRIALS AND EPIDEMIOLOGICAL STUDIES TO RESPOND TO THE CURRENT SCIENTIFIC MEDICAL QUESTION RELATED TO RARE OR HARD TO TREAT CANCERS – PERSONALIZED THERAPY

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3.DEVELOP A DIGITAL COLLABORATION PLATFORM AS SUPPORT OF NCCC TO ACCELERATE THE DIGITAL TRANSFORMATION OF RESEARCH , INNOVATION AND HEALTH SYSTEMS .

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DEVELOPING THE ELECTRONIC FILE OF CANCER PTS  
IMPROVE THE CANCER MANAGEMENT FROM  
DIAGNOSIS TO TREATMENT  
IMPLEMENTATION OF EFFECTIVE PTS ROUTES THAT  
RESPECT EPIDEMIOLOGICAL PRINCIPLES



4.DEVELOPING AND IMPLEMENTING THE “VIRTUAL AND DISTRIBUTED  
TUMOR BOARD” MODULE.

WILL BE DEFINED AND VALIDATED UP TO DATE DIGITALIZED PROTOCOLS  
FOR CANCER TREATMENT BASED ON ESMO AND NCCN, GUIDELINES FOR  
THE LOCALIZATION INCLUDED IN THE NATIONAL PLAN FOR CANCER  
CONTROL LONG BREASTS

USE THE STATE OF THE ART ALGORITHMS OF ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING FOR IMAGE AND VIDEO DATA INTERBRETATION, DATA ANALYTICS , VISUALIZATION AND INCLUDING MOLECULAR DATA WILL BE INTEGRATED IN CLINICAL DECISION.

5. DEVELOPING TUMOR MOLECULAR “BOARD (TMB) SERVICE AS SUPPORT FOR PERSONALIZED MEDICINE BY ANALYZING AND INCLUDING GENETIC AND OMICS DATA IN SELECTING THE MOST SUITABLE TARGETED THERAPY.



THE ROLE OF THE TMB TEAM IS TO GUIDE THE ONCOLOGISTS IN SELECTING AND ASSESSING TREATMENT OPTIONS BASED ON TUMOR SPECIFIC GENETIC AND HISTOLOGIC PHENOTYPES





STATE OF THE ART TECHNOLOGIES ( NGS, MICROARRAY ) AND SPECIFIC CANCER PANELS FOR BOTH GERMINAL AND SOMATIC ALTERATION ( TISSUE / LIQUID BIOPSY ) WILL BE USED

6.


- ASSESMENT OF GENOMIC AND MOLECULAR FACTORS ALONGSIDE SOCIAL DETERMINANTS OF HEALTH FOR ACCURATE ESTIMATION OF INDIVIDUAL DIESEASE RISK



- 
- COMBINATORIAL STUDIES BASED ON CRITICAL INFORMATION FROM DATA BASES FOR IDENTIFYING AND ENGAGING KEY PARTNERS IN PERSONALIZED PRIMARY PREVENTION FOR CANCER
  - DEFINING STRATEGIES TO PERSONALIZE EARLY DIAGNOSIS PROGRAMS TO FACILITATE RESEARCH PROGRAMS
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7.

- DEVELOPING AND INTEGRATED APPROACH BASED ON DIGITAL PATOLOGY AND BIOMARKER PROFILES TO IMPROVE ACCURACY FOR EARLY DIAGNOSIS AND METASTASIS PREDICTION

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- IDENTIFYING NEW BIOMARKERS FOR EARLY DIAGNOSIS, PROGNOSIS AND TREATMENT PREDICTION REPRESENTS A CONTINUOUS CHALLENGE FOR IMPROVING THE MANAGEMENT OF CANCER PTS.
  - NCC CONSORTIUM FOCUSED ON IDENTIFYING NEW SPECIFIC CANCER BIOMARKERS BY SCREENING BOTH TISSUE AND LIQUID BIOPSY SAMPLES

FROM CANCER PREVENTION AND SCREENING MEASURES TO  
PERSONALIZED PATIENT CENTERED STRATEGIES

- FOR CERTAIN ADULT AND PEDIATRIC MALIGNANCIES THROUGH A BETTER UNDERSTANDING OF DISEASE DETERMINANTS
- IS STRUCTURES AROUND 3 FILLARS WHERE IT CAN ADD THE MOST VALUE IN CANCER : PREVENTION ,EARLY DETECTION DIAGNOSIS

## PREVENTION CANCERS CAUSED BY INFECTIONS

- VIRUSES CAN CONTRIBUTE TO THE BIOLOGY OF MULTISTEP ONCOGENESIS
- THE 4 MOST PROMINENT INFECTION – RELATED CAUSES OF CANCER ARE ESTIMATED TO BE VIRAL :
  - HPV
  - HBS
  - HCV
  - EPSTEIN – BARR VIRUS

ADVANCED AND MORE AFFORDABLE HPV DIAGNOSTIC AND TRIAGING ASSAYS ARE NEEDED

- HPV – THE SECOND MOST IMPORTANT INFECTIONS CAUSE OF CANCER WORLDWIDE
- VACCINES USED FOR PROPHYLAXIS OF HPV INF-USED WORLDWIDE FOR MORE THAN 10 YEARS
- INDUCED HIGH LEVELS OF ANTIBODIES FOR AT LEAST 8-10 YEARS

- THE LINKS BETWEEN INF AND CANCER TYPES HAS PROVIDED ACTIONABLE OPPORTUNITIES
- THE USE OF HPV VACCINES AS A PREVENTIVE MEASURE
- FLAGSHIP INITIATIVES OF EUROPE'S BEATING CANCER PLAN IS TO VACCINATE AT LEAST 90% OF THE EU TARGET POPULATION OF GIRLS IN ORDER TO ELIMINATE CERVICAL CANCER AND OTHERS CAUSED BY HPV

## 2. LIVER CANCER HEPATOCELLULAR RANKING AS THE 3<sup>RD</sup> LEADING CAUSE OF CANCER – RELATED CANCER RELATED WORLDWIDE

- THE MAIN RISK FOR HCC OCCURRENCE IS ADVANCED LIVER FIBROSIS (F3- F4 METASTASIS )
- RELATED MAINLY TO VIRAL INFECTIONS (HBV, HDV, HCV) BUT ALSO TO ALCOHOL CONSUMPTION OBESITY , ADVANCED AGE > 65 YEARS , DIABETES MELLITUS SMOKING OTHER METABOLIC FACTORS OR GENETIC VARIANTS.



- EVEN HB RELATED HCC IS DECREASING DUE TO ANTIVIRAL THERAPY AND VACCINATION, IN ROMANIA HBV AND HCV COINFECTION STILL REPRESENTS THE MAIN CAUSE OF LIVER CANCER
- ACCORDING TO PROROK'S POSTULATES HCC SHOULD BE INCLUDED AS CANCERS THAT NEED SCREENING AND SUVEILLANCE

STILL DEFICIENT IDENTIFICATION ,INDENTIFICATION OF USEFUL BIOMARKERS FOR SURVEILLANCE AND EARLY HCC DIAGNOSIS

- SHOWING RATHER LOW SENSIVITY AND HETEROGENEOUS SPECIFICITY
- CIRCULATING TUMOUR CELLS, CtDNA ,OR TUMOUR EDUCATED PLATELETS (TEPS) PROVIDE NOVEL BIOMARKERS EVALUATED IN LIQUID BIOPSIES

- QUANTIFICATION OF ctDNA TOGETHER WITH DETECTION OF DEFINED SOMATIC MUTATIONS COULD BE USED TO FACILITATE EARLY DIAGNOSIS IN HCC
- TERT PROMOTER MUTATIONS C228 AND C250T IS MOST FREQUENT SOMATIC MUTATIONS IN HCC BUT ALSO IN CIRRHOSIS AS A PREMALIGNANT STATE

- THE DETECTION OF TERT PROMOTER MUTATIONS IN LIQUID BIOPSY PLUS OTHER GENETIC AND EPIGENETIC BIOMARKERS COULD DEFINE BETTER THE PREMALIGNANT STATE
- INDICATE A GROUP OF PTS IN WHICH AGGRESSIVE SURVEILANCE FOR HCC IS MANDATORY

REFINE OUR SCORE FOR EARLY DIAGNOSIS ONE OF THE AIMS OF THE PROPOSED RESEARCH GRANT

- THE ADDITION OF THE GENETIC BIOMARKERS COULD FURTHER REFINE OUR SCORE
- THE USE OF GENETIC BIOMARKERS IN LIQUID BIOPSY IS A NOVEL APPROACH TO SCREENING AND SURVEILLANCE IN HCC EMPHASING SENSITIVE TUMORAL MOLECULAR FEATURES SIGNIFICANT FOR EARLY DG AND TARGETED THERAPY

## CREATE A NEW SCORE WITH A SIGNIFICANTLY IMPROVED SENSITIVITY AND SPECIFICITY

- FOR SCREENING IN HIGH RISK POPULATIONS, AS WELL AS AN ALGORITHM FOR PERSONALIZED THERAPY
- THE ADDITION OF GENETIC BIOMARKERS TO GALAD SCORE ( PROVED TO PREDICT EARLY HCC INCLUDES AGE, GENDER AFP + L3 – AFP + DCP )
- USE OF US AND ELASTOGRAPHY

## THE EPSTEIN-BARR VIRUS INFECTION

- IS A KNOWN CANCER CAUSATIVE AGENT
- INCREASING THE RISK OF NASOPHARYNGEAL CANCER, STOMACH CANCER AND CERTAIN TYPES OF LYMPHOMAS SUCH AS BURKITT LYMPHOMA OR HODGKIN LYMPHOMA
- THE MAIN TRIGGER IS PROLONGED CHRONIC INFLAMMATION WITH A STRONG INFLAMMATORY RESPONSE INDUCED BY A MAJOR CD8 + CYTOTOXIC T-CELL INFILTRATE AS A RESULT OF A EBV INFECTION

- THE IMMUNE CHECKPOINT LIGANDS ( PD-L1, PD-L2 ) OVEREXPRESSION CAN BE A VALUABLEWAY TO BLOCK THE PD-1 / PD-L1 PATHWAY, WITH CLEAR BENEFITS OF IMMUNOTHERAPY
- MOREOVER THE EBV CANCERS PRESENT YAK2 OVEREXPRESSION IN THE PIK 3 CA GENE NON-SILENT MUTATIONS



- THESE DATA SUGGEST THAT EBV POSITIVE TUMORS COULD BE TARGETED WITH TYROSINE-KINASE INHIBITOR ( TKI ) SUCH AS P3 KINASE YAK 2 INHIBITORS, OR WITH A COMBINATION OF THOSE 2 TYPES

## IMPROVING EARLY DETECTION ON CANCER THROUGH SCREENING

- KNOWLEDGE GAPS AND IMPLEMENTATION OF NEW CANCER RESEARCH TECHNOLOGIES OF PT CENTERED CANCER PREVENTION AND CARE
- ONE OF THE FLAGSHIP INITIATIVES OF EUROPE'S BEATING CANCER PLAN IS TO PREVENT CANCER MORTALITY AND MORBIDITY THROUGH POPULATION BASED SCREENING

## COLORECTAL CANCER

- SIGNIFICANT CAUSE OF CANCER RELATED MORBIDITY AND DEATH WORLDWIDE
- CRC SCREENING PILOTED BY 2 PROJECTS
  1. SPECIFIC A.I. / MACHINE LEARNING TOOLS WILL BE DEVELOPED AND IMPLEMENTED IN ORDER TO IMPROVE PARTICIPATION IN EXISTING CRC SCREENING AND EARLY DETECTION OF CRC

EXTEND SCREENING TO CANCERS FOR WHICH SCIENTIFIC EVIDENCE  
DEMONSTRATES ADVANTAGES OF EARLY DETECTION

- FURTHER RESEARCH TO COVER GAPS IN KNOWLEDGE ABOUT THE PRECISE CAUSAL ROLE OF MANY ENVIRONMENTAL AND OTHER FACTORS SUCH AS SMOKING FAMILY HISTORY POLLUTION, RADIATION , OCCUPATIONAL EXPOSURE LIFESTYLE, CLIMATE CHANGE
- NEEDED IN ORDER TO IMPROVE THE PREVENTION OF LUNG, CRC, PROSTATE, LIVER CANCER

## 2. LYNCH SYNDROME

- THE MOST COMMON CAUSE OF HEREDITARY CRC IS RESPONSIBLE FOR 3- 5% OF ALL CRC CASES
- IN ROMANIA IS NO CURRENT NATIONWIDE PROTOCOL FOR LS TESTING
- TO ADDRESS THIS GAP WE WILL EVALUATE MOLECULAR TESTING METHODS GENOMIC ANALYSES IN A PILOT STUDY PROVIDING NOVEL INSIGHTS IN THE MOLECULAR SUSCEPTIBILITY FOR CRC

## LUNG CANCER ( LC )

- LEADING CAUSE OF DEATH FROM SOLID TUMORS IN ROMANIA AND THE 3<sup>RD</sup> OF ALL DEATH CAUSES
- RECENT DATA SHOWED A SURVIVAL BENEFIT OF 20% FOR LC SCREENING WITH VARIOUS FALSE POSITIVE RATES OF LOW-DOSE CT (LDCT)

## BETTER SELECT THE POPULATION FOR A NEW SCREENING PROGRAM IN ROMANIA

- INNOVATIVE LC SCREENING BY USING MODERN TOOLS
  - A.i TECHNOLOGY TO BETTER CHARECTERIZE THE LESIONS ON THE LDCT AND TO DEFINE THE CORRELATIONS ALGHORITHM WITH CIRCULATING BIOMARKERS CA 125, CEA CYFRA 21, NSE,PCR,LDH,SCC,LYMPHOCYTES / NEUTROPHIL RATIO, p53, IL-1BETA

## THE COMPLEX DIAGNOSIS MONITORING, EARLY CARE AND PREVENTION OF ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) RELAPSES

- 35% OF ALL CHILD CANCERS
- HETEROGENOUS MALIGNANCIES IN TERMS OF MOLECULAR MECHANISMS IN THEIR ON SET AND PROGRESSION



BETTER MONITORING OF MINIMAL RESIDUAL DISEASE (MRD) BROUGHT HIGHER RATES OF COMPLETE REMISSION (CR)

- ALL PEDIATRIC PTS ARE STAGED ACCORDING TO RISK GROUPS BASED ON CONVENTIONAL CYTOGENETICS AND CLASSIC MOLECULAR PROFILE BUT THESE TECHNIQUES DO NOT REFLECT GENETIC HETEROGENITY

- LONGITUDINAL MONITORING ESTABLISHES CR, PERMITS INDIVIDUALIZED TREATMENT AND RESTAGES THE PATIENT'S RISK GROUP AND PROGNOSIS DURING TREATMENT
- RELAPSE REMAINS THE MOST CHALLENGING PREDICTOR OF PT. OUTCOME

## A NOVEL MRD MONITORING PROTOCOL PROPOSED

- THROUGH GENE REARRANGEMENTS FOR PEDIATRIC PTS WITH ALL AND FOR ALLO-HSCT IN PEDIATRIC AND ADULT PTS

## TO CLARIFY THE RELATIONSHIP BETWEEN MICROBIOME AND ALLO-HSCT

- IT IS IMPORTANT TO DISCUSS THE INTERPLAY BETWEEN DIGESTIVE MICROBIOTA AND THE HOST'S IMMUNE SYSTEM
- WE PROPOSED A NEW APPROACH IN FINDING THE CORRELATION BETWEEN THE MICROBIOME, IMMUNE RECOVERY AND HSCT AND ESTABLISHING BETTER PATIENT'S MANAGEMENT

## OBJETIVES AND METHODOLOGY

- PERSONALIZED RISK ASSESSMENT AND IDENTIFICATION OF BIOMARKERS IN ORDER TO IMPROVE THE ACCURACY AND ACCEPTANCE OF LC SCREENING
- REDUCING THE FINANCIAL BURDEN, OVERDIAGNOSIS, OVERTREATMENT PSYCHOLOGICAL DISTRESS AND RADIATION EXPOSURE THAT COME WITH CONVENTIONAL SCREENING MEASURES

## OBJECTIVES AND METHODOLOGY

- TO IMPROVE PARTICIPATION IN CRC SCREENING IN ROMANIA ESTABLISHING SPECIFIC AI / MACHINE LEARNING RESEARCH TOOLS AND DEVELOPING NEW APPROACHES FOR SCREENING STRATEGY TO THE MOST FREQUENT HEREDITARY CRC CASES

## OBJECTIVES AND METHODOLOGY

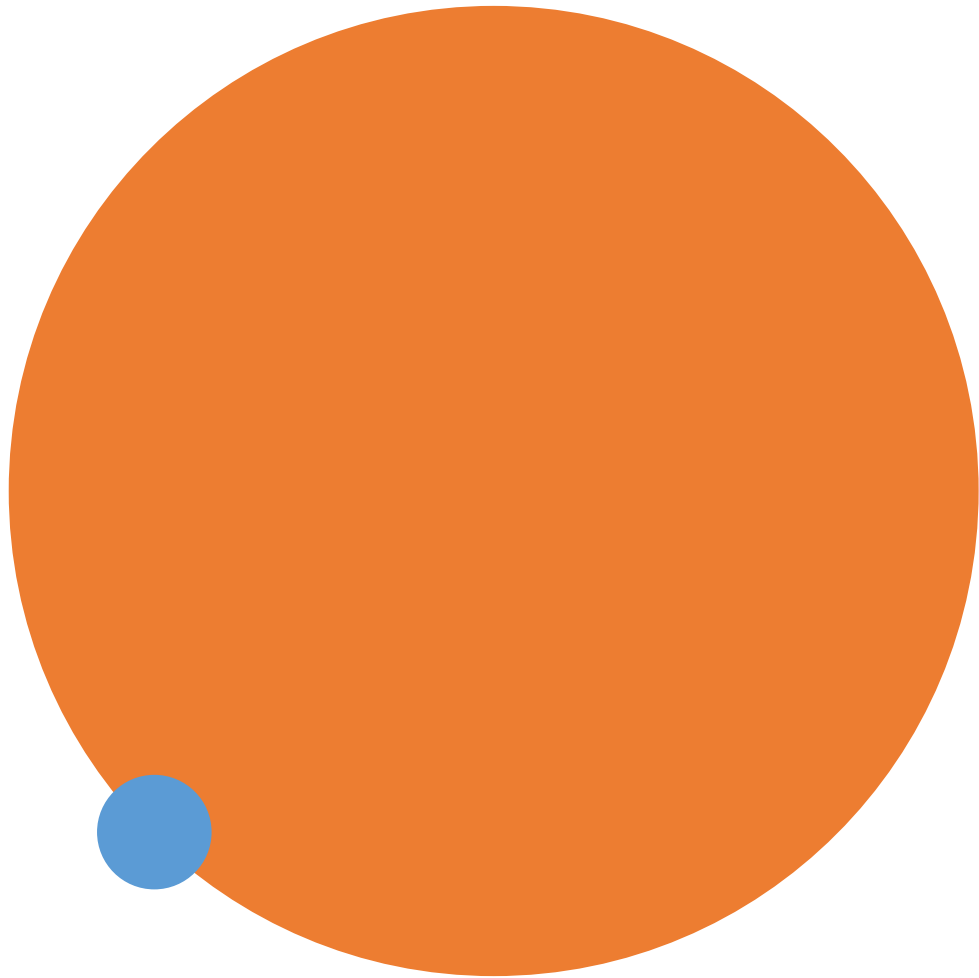
- TO ASSESS THE ADITIVE VALUE OF LIQUID BIOPSY AND COMBINED SEROLOGICAL BIOMARKERS FOR HCC SCREENING EARLY DIAGNOSIS AND THEN SURVEILLANCE AFTER THERAPY FOR IMPROVING OUTCOMES AS WELL AS TO CREATI A PERSONALIZED ALGORITHM FOR TREATMENT DECIDED BY A MULTIDISCIPLINARY RB FOR CONFIRMED HCC BASED ON CLINICAL, RADIOLOGICAL, SEROLOGICAL AND LIQUID BIOPSY BIOMARKERS



8.

- DEVELOPING NEUROIMAGING-BASED PAIN BIOMARKERS FOR PERSONALIZED PAIN THERAPY – USING INTEGRATIVE CLINICAL AND NEUROIMAGING – BASED EVALUATION OF PAIN





- THE PREDICTIVE POTENTIAL OF NEUROIMAGING MARKERS FOR PERSONALIZED PAIN THERAPY WILL BE EVALUATED





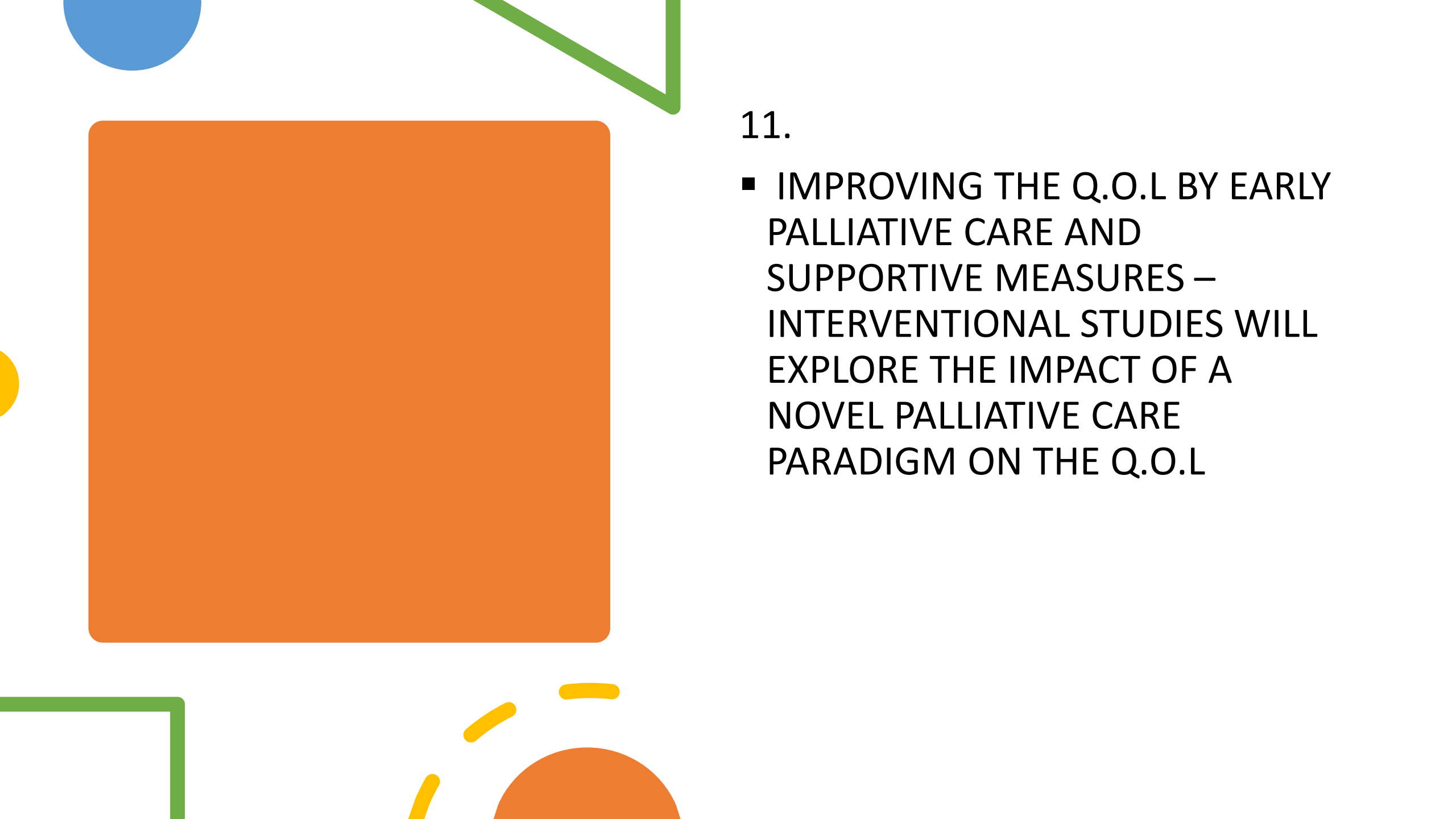
9.

- IMPROVING THE QUALITY OF CANCER CARE BY COMPREHENSIVE EVALUATION OF THE HEALTHCARE EXPERIENCE OF PTS WITH CANCER
  - WILL BE PERFORMED USING A NOVEL QUESTIONNAIRE BASED ON FORMATIVE RESEARCH
-

10.


- TO EVALUATE THE ROLE OF POSITIVE HEALTHCARE EXPERIENCE IN IMPROVING THE Q.O.L

- FACTORS WHICH DETERMINE POSITIVE EXPERIENCE FOR PTS WILL BE IDENTIFIED



11.

- IMPROVING THE Q.O.L BY EARLY PALLIATIVE CARE AND SUPPORTIVE MEASURES – INTERVENTIONAL STUDIES WILL EXPLORE THE IMPACT OF A NOVEL PALLIATIVE CARE PARADIGM ON THE Q.O.L





11.

- IMPROVING THE Q.O.L BY EARLY PALLIATIVE CARE AND SUPPORTIVE MEASURES – INTERVENTIONAL STUDIES WILL EXPLORE THE IMPACT OF A NOVEL PALLIATIVE CARE PARADIGM ON THE Q.O.L
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12.

- DISSEMINATION OF RESEARCH RESULTS, SUPPORT ACTIVITIES AND THE IMPLEMENTATION OF THE OBJECTIVES, OF THE EU MISSIONS OF CANCER WITH IN HORIZON EUROPE IN ROMANIA

- A WEB PAGE WITH ALL DEVELOPED PROTOCOLS
- PERIODICALLY COMMUNICATION TO A LARGER AUDIENCE THROUGH SOCIAL MEDIA, TV AND PRESS REALEASES

- 
- A SCIENTIFIC HUB WILL BE DEVELOPED FOR BRINGING NEW DATA, FOR IDENTIFYING NEW BIOMARKERS FOR EARLY DIAGNOSIS AND TREATMENT PREDICTION
  - BY COLLABORATION WITH ALL PARTNERS FROM CONSORTIUM
  - FOR IDENTIFYING THE NEW OPPORTUNITY AND FUNDING GRANTS FOR EXTENDING THE PNCC NETWORK TO FUTURE PARTNERS
- 





- THE N.C.C.C. CONSORTIUM WILL PROPOSE AT LEAST ONE PROJECTS PROPOSAL DURING HORIZON EUROPE- WORK PROGRAMME

2023-2024

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