** **

***“BANDO PROGETTO SPECIALE 2017 SU PATOLOGIE AMIANTO-CORRELATE”***

**ANNUAL SCIENTIFIC REPORT**

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# GENERAL INFORMATION

* *Project number:* **ARL\_2/2018**
* *Project acronym:* **PRIMATE**
* *Project title:* **An integrated precision medicine approach to malignant mesothelioma: from mutation load to epidemiology and therapy**
* *Start date:* **01-01-2018**
* *Project duration (in months):* **36+5**
* *Name of the project’s coordinator:* **Prof: Tommaso Dragani**
* *Organization of the project's coordinator:* **Fondazione IRCCS Istituto Nazionale dei Tumori, Milan**
* *Period covered by the report:* **from 01-01-21 to 31-12-21**

# DELIVERABLES

|  |  |  |
| --- | --- | --- |
| **Deliverables** | **Timing** | **Accomplished** |
|  | month | YES | NOT YET | ABANDONED |
| **D1**: collection of a few slices of MM FFPE tissue samples and the non-tumor counterpart of 1,000 cases | 12 |  |  |  |
| **D2**: quantification of the asbestos bodies in non-involved lung tissue of 500 certified MM cases; association of asbestos body counts with patient’s OS and age at diagnosis | 12 |  |  |  |
| **D3**: collection of MM tissues in RNAlater, for patients who will have been treated by surgery, or a few slices of FFPE tissue samples, for inoperable patients, for a total of 150 cases | 30 |  |  |  |
| **D4**: collection of 80 blood samples from MM cases | 30 |  |  |  |
| **D5**: identification of immune markers associated with OS, age at diagnosis and therapy | 36 |  |  |  |
| **D6**: identification of somatic mutations in the coding portion of the genome that are peculiar to MM and significantly associated with OS, age at diagnosis, therapy, and asbestos body count of MM patients | 36 |  |  |  |
| **D7**: whole genome genotyping and identification of SNPs associated with clinical parameters, such as age at diagnosis, OS, therapy or asbestos body count | 36 |  |  |  |
| **D8**: identification and quantification of metabolites and cytokines in the plasma of MM patients, associated with age at diagnosis, OS, therapy, or asbestos body count | 36 |  |  |  |
| **D9**: identification of integrated networks of MM biomarkers | 36 |  |  |  |
| **D10**: indications of feasibility and assessment of biomolecular effects of BNCT for MM and definition of the characteristics of new boronated formulations, necessary to ensure a high cellular uptake | 36 |  |  |  |
| **D11**: a database with complete information on the patients’ exposure history | 36 |  |  |  |
| **D12**: quantitative correlation between asbestos body burden and exposure estimation and identification of major determinants for exposure assessment when asbestos body burden is not available | 36 |  |  |  |
| **D13**: quantitative measures of association between objective measures of asbestos exposure and somatic mutations and plasma inflammatory markers | 36 |  |  |  |
| **D14**: New sources of evidence for the current legal debates and practices on causation in asbestos trials; new guide lines for judges and lawyers who are called to deal with the issue of causal links between multiple exposure and the occurrence or the development of MM | 36 |  |  |  |

# WORK PACKAGES

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| --- |
| **WP1: Retrospective mesothelioma series collection** |

### **AIM 1: Collection of mesothelioma formalin-fixed, paraffin-embedded (FFPE) samples**

#### Partners involved

*Flag the box of the partner/s involved in this Aim*

|  |  |
| --- | --- |
| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
| Partner 1 | Università degli Studi di Milano, Milan |  |
| Partner 2 | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan |  |
| Partner 3 | Istituto Clinico Humanitas, Rozzano (MI) |  |
| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

|  |
| --- |
| *max ½ page* |

### **AIM 2: Collection of non-involved lung tissue samples from MM patients**

#### Partners involved.

*Flag the box of the partner/s involved in this Aim*

|  |  |
| --- | --- |
| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
| Partner 1 | Università degli Studi di Milano, Milan |  |
| Partner 2 | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan |  |
| Partner 3 | Istituto Clinico Humanitas, Rozzano (MI) |  |
| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results.

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

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| *max ½ page* |

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| **WP2: Prospective mesothelioma series collection** |

### **AIM 1: Collection of FFPE or RNAlater samples from MM patients**

#### Partners involved.

*Flag the box of the partner/s involved in this Aim*

|  |  |
| --- | --- |
| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
| Partner 1 | Università degli Studi di Milano, Milan |  |
| Partner 2 | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan |  |
| Partner 3 | Istituto Clinico Humanitas, Rozzano (MI) |  |
| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results.

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

|  |
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| *max ½ page* |

### **AIM 2: Collection of blood samples**

#### Partners involved.

*Flag the box of the partner/s involved in this Aim*

|  |  |
| --- | --- |
| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
| Partner 1 | Università degli Studi di Milano, Milan |  |
| Partner 2 | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan |  |
| Partner 3 | Istituto Clinico Humanitas, Rozzano (MI) |  |
| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results.

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

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| **WP3: Molecular analyses** |

### **AIM 1: Immunohistochemical analysis of MM microenvironment**

#### Partners involved.

*Flag the box of the partner/s involved in this Aim*

|  |  |
| --- | --- |
| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
| Partner 1 | Università degli Studi di Milano, Milan |  |
| Partner 2 | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan |  |
| Partner 3 | Istituto Clinico Humanitas, Rozzano (MI) |  |
| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results.

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

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### **AIM 2: Identification of somatic mutations by whole exome sequencing (WES)**

#### Partners involved.

*Flag the box of the partner/s involved in this Aim*

|  |  |
| --- | --- |
| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
| Partner 1 | Università degli Studi di Milano, Milan |  |
| Partner 2 | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan |  |
| Partner 3 | Istituto Clinico Humanitas, Rozzano (MI) |  |
| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results.

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

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### **AIM 3: Identification of germline variants by genome-wide single nucleotide**

#### Partners involved.

*Flag the box of the partner/s involved in this Aim*

|  |  |
| --- | --- |
| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
| Partner 1 | Università degli Studi di Milano, Milan |  |
| Partner 2 | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan |  |
| Partner 3 | Istituto Clinico Humanitas, Rozzano (MI) |  |
| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results.

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

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### **AIM 4: Identification of plasma inflammatory biomarkers**

#### Partners involved.

*Flag the box of the partner/s involved in this Aim*

|  |  |
| --- | --- |
| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
| Partner 1 | Università degli Studi di Milano, Milan |  |
| Partner 2 | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan |  |
| Partner 3 | Istituto Clinico Humanitas, Rozzano (MI) |  |
| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results.

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

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### **AIM 5:Integration of -omic data for the identification of networks of biomarkers in MM**

#### Partners involved.

*Flag the box of the partner/s involved in this Aim*

|  |  |
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| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
| Partner 1 | Università degli Studi di Milano, Milan |  |
| Partner 2 | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan |  |
| Partner 3 | Istituto Clinico Humanitas, Rozzano (MI) |  |
| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results.

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

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### **AIM 6: Investigation of new therapeutic strategies for the treatment of MM by boron neutron capture therapy (BNCT) in cell cultures**

#### Partners involved.

*Flag the box of the partner/s involved in this Aim*

|  |  |
| --- | --- |
| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
| Partner 1 | Università degli Studi di Milano, Milan |  |
| Partner 2 | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan |  |
| Partner 3 | Istituto Clinico Humanitas, Rozzano (MI) |  |
| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results.

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

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| *max ½ page* |

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| **WP4: Retrospective assessment of exposure to asbestos fibers** |

### **AIM 1: Collection, organization and ranking of available information on patients’ exposure to asbestos**

#### Partners involved.

*Flag the box of the partner/s involved in this Aim*

|  |  |
| --- | --- |
| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
| Partner 1 | Università degli Studi di Milano, Milan |  |
| Partner 2 | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan |  |
| Partner 3 | Istituto Clinico Humanitas, Rozzano (MI) |  |
| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results.

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

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### **AIM 2: Retrospective exposure assessment (REA)**

#### Partners involved.

*Flag the box of the partner/s involved in this Aim*

|  |  |
| --- | --- |
| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
| Partner 1 | Università degli Studi di Milano, Milan |  |
| Partner 2 | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan |  |
| Partner 3 | Istituto Clinico Humanitas, Rozzano (MI) |  |
| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results.

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

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| **WP5: Epidemiological and legal aspects** |

### **AIM 1: Definition of the relation between characteristics of MM and objective measures of asbestos body burden**

#### Partners involved.

*Flag the box of the partner/s involved in this Aim*

|  |  |
| --- | --- |
| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
| Partner 1 | Università degli Studi di Milano, Milan |  |
| Partner 2 | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan |  |
| Partner 3 | Istituto Clinico Humanitas, Rozzano (MI) |  |
| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results.

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

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### **AIM 2: The proof of causation in asbestos trials: filling evidence gaps through the characterization of MM**

#### Partners involved.

*Flag the box of the partner/s involved in this Aim*

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| --- | --- |
| Partners involved | ✔ |
| Coordinator | Fondazione IRCCS Istituto Nazionale dei Tumori, Milan |  |
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| Partner 4 | Università degli Studi dell'Insubria, Como |  |

#### Obtained results.

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| *max ½ page (plus figures and tables if present)* |

#### Pitfalls and caveats and how they have been overcome, or possible solutions to overcome them.

|  |
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| *max ½ page* |

# DISSEMINATION

## Exploitation of results

*Type of Dissemination: Organization of a Conference, Organization of a workshop, Press release, Non-scientific and non-peer reviewed publications, Exhibition, Flyers, Social media, Website, Communication campaign (e.g. radio, TV), Participation in a conference, Participation in a workshop, Participation in an event other than a conference or workshop, etc.*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Type of Dissemination | Partner (s) | Date | Where | Link |
|  |  |  |  |  |
|  |  |  |  |  |
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## Scientific publications

*Please note: only publications acknowledging FRRB funding shall be listed*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| TypeR: reviewP: paper | Title of the scientific publication | DOI | Partner(s) involved | Journal title | Year | Open AccessYES/NO | Journal IF |
|  |  |  |  |  |  |  |  |
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|  |  |  |  |  |  |  |  |

*IMPORTANT: Please report all the publications also in the excel file “Publications” specifying:*

* *Title*
* *Year*
* *Journal and related Impact factor*
* *Partners involved*
* *Members of the team supported by FRRB among the authors*
* *In case of other source of funding declared in the acknowledgments, specify very briefly which aspects of the published work have been developed with the FRRB funding or with other funds of the PIs*

# EXPLANATION ON THE USE OF RESOURCES

## **COORDINATOR: Fondazione IRCCS Istituto Nazionale dei Tumori, Milan**

Total amount reported in the Cost Statement Year 3 (overheads included): € \_\_\_\_\_\_\_\_\_\_\_\_\_

Explanation

|  |
| --- |
| *Please provide an explanation of any major direct costs incurred by the beneficiary in this reporting period (personnel costs, purchase of important equipment, travel costs, large consumable items, etc.) and describe any relevant variation compared to the initial approved financial plan (*max ½ page) |

Gender issues

*Please, provide information about the research team members that have been recruited in the context of this project*

|  |  |  |
| --- | --- | --- |
| Role(PhD student, postdoc, technician, etc.) | Type of contract(temporary or permanent) | GenderW: womanM: manO: other/no answer |
|  |  |  |
|  |  |  |
|  |  |  |

## **PARTNER 1: Università degli Studi di Milano, Milan**

Total amount reported in the Cost Statement Year 3 (overheads included): € \_\_\_\_\_\_\_\_\_\_\_\_\_

Explanation

|  |
| --- |
| *Please provide an explanation of any major direct costs incurred by the beneficiary in this reporting period (personnel costs, purchase of important equipment, travel costs, large consumable items, etc.) and describe any relevant variation compared to the initial approved financial plan (*max ½ page) |

Gender issues

*Please, provide information about the research team members that have been recruited in the context of this project*

|  |  |  |
| --- | --- | --- |
| Role(PhD student, postdoc, technician, etc.) | Type of contract(temporary or permanent) | GenderW: womanM: manO: other/no answer |
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## **PARTNER 2: Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, MILAN**

Total amount reported in the Cost Statement Year 3 (overheads included): € \_\_\_\_\_\_\_\_\_\_\_\_\_

Explanation

|  |
| --- |
| *Please provide an explanation of any major direct costs incurred by the beneficiary in this reporting period (personnel costs, purchase of important equipment, travel costs, large consumable items, etc.) and describe any relevant variation compared to the initial approved financial plan (*max ½ page) |

Gender issues

*Please, provide information about the research team members that have been recruited in the context of this project*

|  |  |  |
| --- | --- | --- |
| Role(PhD student, postdoc, technician, etc.) | Type of contract(temporary or permanent) | GenderW: womanM: manO: other/no answer |
|  |  |  |
|  |  |  |
|  |  |  |

## **PARTNER 3: Istituto Clinico Humanitas, Rozzano (MI)**

Total amount reported in the Cost Statement Year 3 (overheads included): € \_\_\_\_\_\_\_\_\_\_\_\_\_

Explanation

|  |
| --- |
| *Please provide an explanation of any major direct costs incurred by the beneficiary in this reporting period (personnel costs, purchase of important equipment, travel costs, large consumable items, etc.) and describe any relevant variation compared to the initial approved financial plan (*max ½ page) |

Gender issues

*Please, provide information about the research team members that have been recruited in the context of this project*

|  |  |  |
| --- | --- | --- |
| Role(PhD student, postdoc, technician, etc.) | Type of contract(temporary or permanent) | GenderW: womanM: manO: other/no answer |
|  |  |  |
|  |  |  |
|  |  |  |

## **PARTNER 4: Università degli Studi dell'Insubria, Como**

Total amount reported in the Cost Statement Year 3 (overheads included): € \_\_\_\_\_\_\_\_\_\_\_\_\_

Explanation

|  |
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| *Please provide an explanation of any major direct costs incurred by the beneficiary in this reporting period (personnel costs, purchase of important equipment, travel costs, large consumable items, etc.) and describe any relevant variation compared to the initial approved financial plan (*max ½ page) |

Gender issues

*Please, provide information about the research team members that have been recruited in the context of this project*

|  |  |  |
| --- | --- | --- |
| Role(PhD student, postdoc, technician, etc.) | Type of contract(temporary or permanent) | GenderW: womanM: manO: other/no answer |
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