BioRAIDs European study in cervical cancer: Study Design

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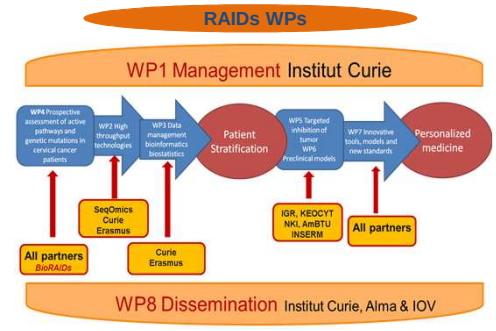
RAIDs: Rational molecular Assessment Innovative Drug Selection : 7 EU countries

Background

Cervical cancer (CC) is the second most common malignancy in women worldwide. High-risk HPV is s an important initiating event in tumor genesis.CC exhibits differences in clinical behavior and stratification of CC into subclasses for progression and response to treatment remains to be defined.
RAIDs is a multidisciplinary co-operation between academic clinical centers, SMEs and translational research platforms. It combines Next Generation Sequencing (NGS) and Reverse Phase Protein array (RPPA) in a large patient population prior to standard therapy.
It includes:
1. a cognitive cohort study (**BioRAIDs**) intended to define patient stratification for targeted therapies
2. targeted clinical trials using an HPV directed vaccine trial or direct viral targeting in association with standard therapy and
3. preclinical studies using cell lines and mouse models to identify new molecules of relevance for CC or CC microenvironment targeting.



BioRAIDs: Patient selection & Study Design

Methodology

BioRAIDs "Biomarker evaluation in advanced stage cervical cancer by an international working group-tumor Stages (1B2 – 4)". 700 Patients - 7 European countries (> 25 centers) will receive primary "standard" treatment. Frozen and fixed biopsies as well as serum/plasma samples are collected before and after treatment in case of residual disease for molecular and proteomics analysis.

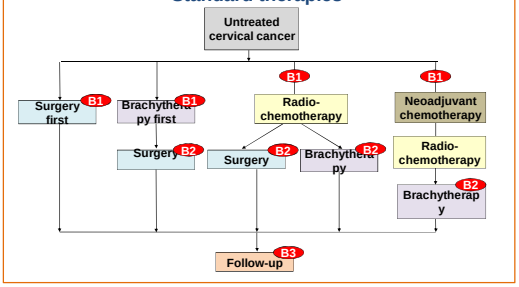
Primary Objective :

Assessment of dominant mutations and activation of signaling pathways which may allow to predict treatment response.

Secondary Objectives :

- Evaluation of the PFS at 18 months in correlation with dominant genetic and protein alterations.
- Descriptive analysis of standard treatment modalities which are applied in the participating EU countries.
- Descriptive analysis of adverse events (grade 3 and 4).
- Descriptive analysis of the frequency and geographic distribution of dominant molecular alterations.

Standard therapies



Inclusion criteria:

1) No prior treatment for cervical cancer.
2) FIGO Stage IB2 to IVB; all histological subtypes (excluding neuro-endocrine type).
3) IRM confirmed cervical lesion & lesion measurable by T2 (MRI must be performed using ultrasound gel in vagina).
4) Possibility to communicate imaging data by CD ROM (format DICOM 3.0 or more).
5) Disease amenable to biopsy (3 tumour samples are mandatory prior to treatment).
6) Age ≥ 18 years.
7) ECOG 0-2.
8) Life expectancy > 6 months.
9) Patient eligible for standard treatment (according to standards of each center).
10) Patient having health care insurance.

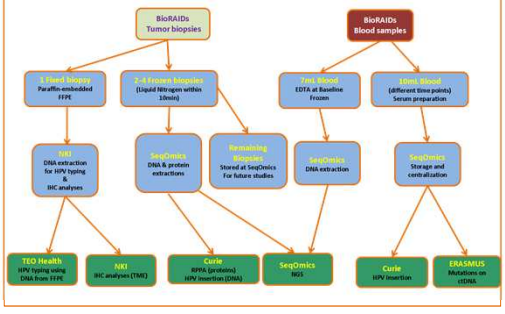
Non-inclusion criteria:

1) Patient enrolled in a clinical trial involving an investigative new agent.
2) Co morbidity, preventing patient to tolerate the proposed standard treatment*.
3) Past history of invasive cancer over the 5 years preceding entry in the present trial (except basal cell carcinoma and carcinoma in situ of the cervix).
4) Impossibility to carry out evaluation by MRI (patient claustrophobic, pacemaker, metallic implant, non availability, other).
5) Patient deprived from the ability to decide on her own.
6) Patient unable to have a regular follow up for geographical, social or psychological reasons.
7) Pregnancy or patient old enough to procreate and not using effective contraceptive method.

Samples

		Before treatment	End of treatment	Poor response	Residual disease, local recurrence or distant progression	6 months after end of treatment	12 months after end of treatment	18 months after end of treatment
Clinical examination		X	X			X	X	X
Gynaecological examination		X	X			X	X	X
Imaging	Scanner	X	x*			x*	x*	x*
	Pelvic MRI	X	X			x*	x*	x*
	PET scan	X				x*	x*	x*
Tumor sampling (Biopsies)	FFPE (formalin)	X (1 min)						
	Frozen	X (2 min)		X (2)	X (2)			
Blood sampling	7ml on EDTA	X						
	10ml in dry tube for serum	X	X	X	X	X	X	X

Samples and Techniques



Conclusions and expected results

RAIDs aims to define a set of stratification criteria based on molecular profiling. Its results should give insight into dominant genomic and protein signalling pathway alterations, enabling the identification of prognostic and predictive biomarkers for standard or targeted therapy in CC. Immunological data from trials involving vaccine or direct viral targeting will provide information on immune rejection or tolerance of this virally transmitted disease.
The RAIDs consortium aims
- to provide a safer and more efficient therapy for the individual patient;
- to raise awareness in countries with lesser screening practices;
- to improve the quality of life for women with cancer via:

a) the acquisition of defined molecular data for better treatment decisions,
b) targeted pilot trials directed at specific alterations and
c) the continuous evaluation of standards of care by comparing standards and outcome in all the RAIDs centres
d) in concertation with other (EORTC and ENGOT) centres and international societies [ESGO (European society for gynaecological oncology) and IGCS (International gynae cancer society)] who may wish to join this initiative in Europe.

BioRAIDs: Expected patients' inclusions