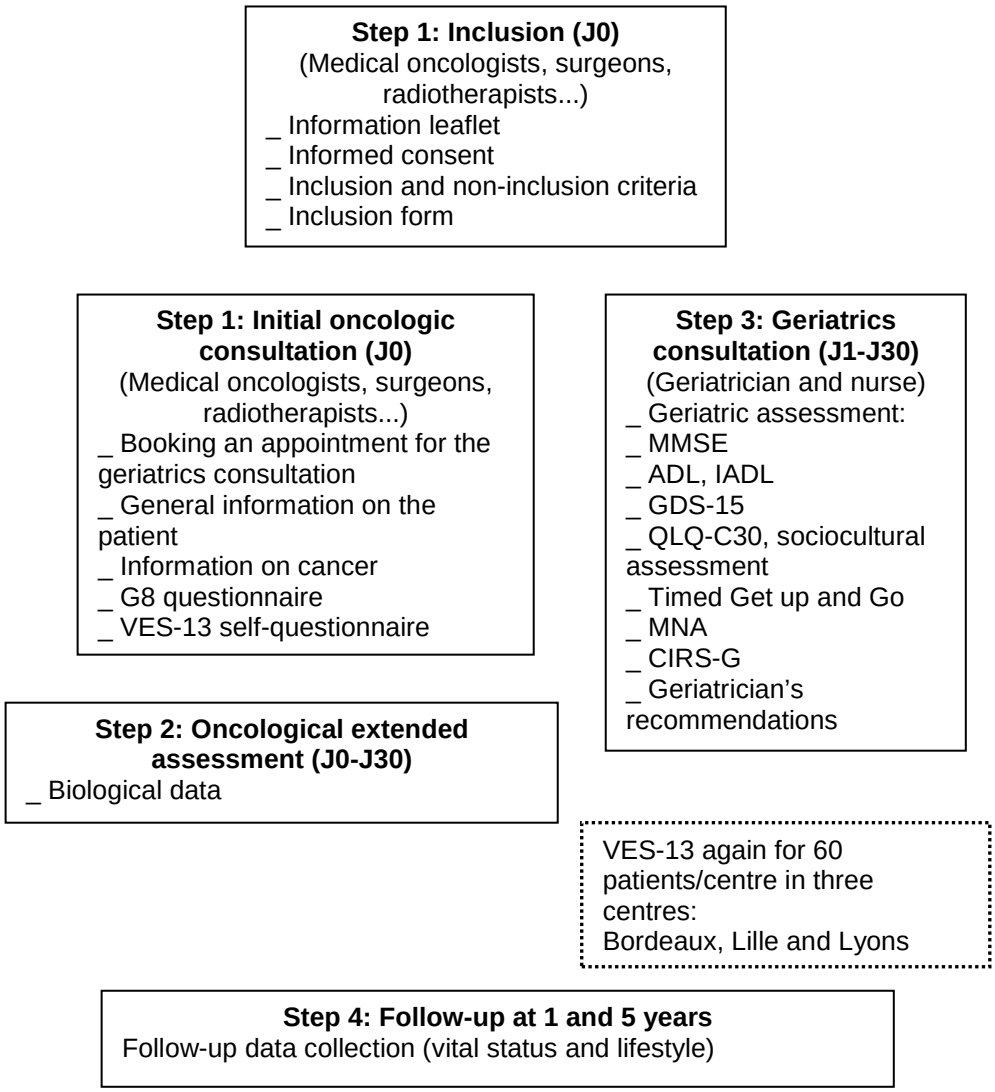
Study title	Validation of a geriatric screening tool in oncology
Acronym	**ONCODAGE**
Coordinating centre	Institut Bergonié, Centre de Lutte Contre le Cancer, Bordeaux.
Coordinator	Pr. Pierre Soubeyran
Number of centres	At least 15: the 15 Pilot Units of Coordination in Geriatric Oncology (*UPCOG*) along with health institutions members of the oncology network.
Indication	Patients over 70 years old with a cancer (colon, lung, ENT, breast, prostate, lymphoma), as part of the initial management.
Trial rationale	As patients age, risks for serious toxicity, or even lethality, during cancer treatment increase. A detailed assessment of the patient's status is required. Comprehensive geriatric assessment (CGA) is a method which has proved its usefulness but which is time-consuming and expensive to administer. A screening tool allowing the individualisation of patients who would benefit from a CGA is necessary. In a previous regional prospective multicentre cohort (regional Ministry of Health-financed project, PHRC 2003), we studied patients over 70 years with cancers who were receiving first-line chemotherapy. This study enabled us to perform an exploratory study in order to develop a screening tool, the G8, which consists of a 7-item questionnaire from the Mini Nutritional Assessment (MNA) and an age indication. We applied the suggested screening tool to our population of 364 patients and this analysis provided encouraging results to be studied on a wider scale (Bellera et al., Ann Oncol, 2012).
Expected effects	With the use of this simple tool for screening, to be administered by nurses or oncologists, we consider that more elderly patients with cancer will be able to benefit from a CGA. This tool will also enable us to rationalise the use of our geriatric assessment means and thus to focus their use on those who need it more, for more efficacy.
Main objective	Validate a new screening tool, the G8, to identify within a population of over 70-year-old patients with cancer those who need further geriatric assessment.
Secondary objectives	– **Validate the French version of the Vulnerable Elders Survey screening tool (VES-13).** – For each suggested screening tool, G8 and VES-13: • Assess the intrinsic qualities of the screening tool (internal consistency, reproducibility, and predictive value), • Assess the screening tool for specific populations (type of cancer, therapeutic strategy, stage of the disease). – Assess the number and type of suggested interventions according to the CGA – Compare both new suggested tools (VES 13 and G8). – Define standards for tests and questionnaires used, for which no standards are currently available (G8, VES-13, MMSE, Timed up and Go, QLQ-C30) in a French population of elderly patients with cancer.
Study design	National multicentre prospective cohort study proposed to the 15 UPCOG and to health institutions member of oncology networks.

Number of patients	In order to ensure a minimum of 1500 assessable patients, we will recruit **1650 patients**.
Inclusion criteria	1. Patients 70-years-old or older 2. Cancer proved histologically, irrespective of grade or stage 3. One of the following tumour types: colon, lung, ENT, breast, and lymphoma, 4. Treated as part of an initial therapeutic management: medical (chemotherapy, hormone therapy, targeted treatment), surgical, or radiotherapeutic 5. Management by one of the 15 UPCOG or teams associated with the project 6. Patients who received the information leaflet and signed the informed consent form 7. Patients registered with a social security coverage
Non-inclusion criteria	1. Persons deprived of freedom or under tutelage 2. Presence of a psychological, familial, social, or geographic condition which might disturb the right course of the study
Study outline	**Oncological assessment consultation** *(oncologist and nurse)* – Information leaflet and informed consent – Assessment of eligibility criteria – Standard clinical examination (oncologist) – G8 questionnaire (oncologist) – VES-13 self-questionnaire (nurse) – Organisation of appointments for oncological assessment (pre-therapeutic evaluation, extended assessment), and geriatric oncologic assessment. **Oncological assessment** The oncological assessment is the extended and standard pre-therapeutic assessments usually performed for patients. Clinical and paraclinical data will be collected for the study. **Geriatric oncologic assessment** *(geriatrician and geriatric assessment nurse for UPCOG)* To be undertaken before starting the oncological treatment and before setting up specific management, within two weeks at least after the oncological assessment consultation. The nurse (IEG) will: – Fill in the ADL, IADL, and MNA questionnaires, along with the socio-cultural assessment score – Administer the MMS and Timed Get up and Go tests – Fill in the GDS-15 and QLQ- C30 self-questionnaires The geriatrician will then see the patient for a geriatrics oncology consultation and will be in charge of completing the CIRS-G questionnaire, the synthesis of the self-questionnaires, the oncological geriatrics assessment, and of the clinical file. S/he should try to identify patients for whom personalised programmes of geriatric interventions are required. **It is essential for the geriatrician not to have access to the G8 or VES-13 results.** **Follow-up** Patients will be followed-up over 5 years. Data collection will be done at 1 and 5 years in order to collect data on vital status, disease progression, and lifestyle (ambulatory, institutionalised).

Summary of



Assessment criteria

Principal assessment criteria

G8 assessment will be performed using as a gold-standard tool the complete CGA based on the following tests, questionnaires, and scales: CIRS-G, ADL and IADL scales Timed Get up and Go test, MNA, MMS, and GDS-15.

Especially, we will consider a patient as being at risk or requiring a complete CGA if we observe at least one of the following conditions:

- CIRS-G: at least one grade ≥ 3 comorbidity (except treated cancer),
- ADL scale: a score below or equal to 5,
- IADL scale: a score below or equal to 7,
- Timed Get up and Go test: time strictly over 20 seconds,
- MNA: a score below or equal to 23.5,
- MMSE: a score below or equal to 23,
- GDS-15: a score over or equal to 6.

These assessments will be performed blindly from the G8 and VES-13 results.

We will assess, for various thresholds of the assessed tool, the performances of the new screening tool compared to the reference one, thanks to the following parameters:

The sensitivity (Se), defined by the proportion of patients registered as "requiring an CGA" with the screening tool, among patients having at least one abnormal CGA element;

The specificity (Sp), defined by the proportion of patients registered as "not requiring a CGA" with the screening tool, among patients "having no abnormal CGA element";

Youden's index (J), summarising the sensitivity and the specificity: J = Se + Sp – 1.

The positive predictive value (PPV), defined by the proportion of patients "having at least one abnormal CGA element", among patients registered as "requiring a CGA" with the screening tool.

The negative predictive value (NPV), defined by the proportion of patients registered as "having no abnormal CGA element", among patients "not requiring a CGA" with the screening tool;

The positive diagnostic likelihood ratios (DLR+), defined by the ratio of positive tests in patients with the disease (true positive) out of positive tests in disease-free patients (FN of false positive).

The negative diagnostic likelihood ratio (DLR-), defined by the ratio of negative tests in patients with the disease (false negative) out of negative tests in disease-free patients (true positive).

The area under the ROC curve will help determining the overall efficacy of the assessed test and determining the threshold value to increase simultaneously sensitivity and specificity of the new screening tool, or to maximise sensitivity while maintaining satisfactory specificity. We will try to maximise sensitivity in order to decrease the G8 false negative rates, patients who would thus be excluded from receiving the best subsequent management.

Secondary assessment criteria

- The validation of the French version of the VES-13 screening tool will be based on the same validation criteria than for G8 tool.
- The assessment of the intrinsic qualities of G8 and VES-13 tools will be based on the accuracy (internal consistency, reproducibility) and validation assessment.
- The assessment of screening tools in various clinical situations will be based on the estimation of sensitivity, specificity, and of predictive values of each

	screening tool according to: • the type of cancer, • the therapeutic strategy (locoregional, and locoregional and adjuvant treatment), • the stage of the disease (local, metastasis). – We will evaluate the number of interventions according to the CGA (change of the initial treatment irrespective of its nature, interventions of other specialists in other fields).
Hypotheses and statistical analyses	**Hypotheses and required number of patients** The objective is to maximise the sensitivity of the new screening tool and to obtain an estimation of sensitivity with satisfactory accuracy. Our exploratory study suggests (section 8) a sensitivity of about 90% when we use as gold standard the presence of an abnormal score for at least one questionnaire, and a prevalence of 50% of patients with at least one abnormal questionnaire. The inclusion of 1500 patients would help estimating the sensitivity on a 750-patient sample with abnormal CGA, with an accuracy of 2.4% for an expected sensitivity of 90% (*i.e.* 95% CI of 87.6% to 92.4%). In order to ensure a minimum of 1500 assessable patients, we will recruit **1650 patients**. **Statistical analyses** The population of the study will be described broadly according to its clinical and sociodemographic characteristics in terms of size and ratio for the qualitative variables and in terms of distribution for the quantitative ones. The following parameters will be estimated: – The sensitivity, the specificity, and the predictive values will be estimated. 95% CIs will be reported (binomial distribution). – The ROC curve representing graphically the sensitivity according to the (1 - specificity) for various thresholds of the assessed test will be represented graphically and help determine the area under the curve (AUC). – Internal consistency will be assessed according to Cronbach's alpha coefficient. A 95% CI will be reported. – Reproducibility will be assessed by the intraclass correlation coefficient for quantitative variables. For qualitative variables, reproducibility will be assessed by Cohen's kappa. – Scores between acknowledged subgroups will be compared thanks to a variance analysis. – Both G8 and VES-13 questionnaires will be compared using their respective area under the curve. – We will assess whether using both screening tools together (G8 and VES-13) helps to obtain a more effective screening tool compared to the sole use of one questionnaire.
KEY DATES	26/03/2008 Initial ethics application 14/05/2008 Scientific board meeting (am) Investigators meeting (pm) 27/05/2008 AFSSAPS Authorisation 05/08/2008 Beginning of inclusions 08/09/2009 Scientific board meeting

	16/10/2009 IDMC 08/03/2010 End of inclusions 22/02/2010 to 14/09/2010 Monitoring onsite (19 sites / 528 files / 32% of included patients) 15/09/2010 to 12/10/2010 Preliminary analysis 13/10/2010 Preliminary results presentation (INCa + scientific board) 01/11/2010 to 31/01/2011 Finalisation of analyses (except for the follow-up analysis) **31/01/2011 Final report n°1** 30/04/2011 Follow-up data at 1 year available for all patients 01/05/2011 to 30/05/2011 Follow-up data analyses at 1 year 30/04/2015 Follow-up data at 5 years available for all patients 01/05/2015 to 30/05/2015 Follow-up data analyses at 5 years