VOLUME 27 · NUMBER 26 · SEPTEMBER 10 2009

JOURNAL OF CLINICAL ONCOLOGY

CORRESPONDENCE

# 2009 Version of the Chompret Criteria for Li Fraumeni Syndrome

**TO THE EDITOR:** We read with great interest the article by Gonzalez et al[1] published in *Journal of Clinical Oncology*. This study confirms the clinical utility of the Chompret criteria, which the French Li Fraumeni syndrome (LFS) working group elaborated in 2001 to facilitate diagnosis of LFS.[2] Gonzalez et al performed *TP53* analysis in 341 clinically informative families, including 195 families fulfilling the Chompret criteria; obtained a mutation detection rate of 35% (69 of 195 families); and estimated the sensitivity and specificity of these criteria to be 92% and 53%, respectively. The authors were seemingly not aware of our study[3] published last year, which had already validated the clinical utility of these criteria. We analyzed *TP53* in 474 French families suggestive of LFS, including 232 families fulfilling the Chompret criteria; obtained a mutation detection rate of 29% (67 of 232 families); and estimated the sensitivity and specificity of the Chompret criteria to be 82% and 58%, respectively. We also proposed extending the Chompret criteria to cover the clinical presentation of the 82 families in which we identified germline *TP53* mutations. The extended criteria would include the following: A proband with a tumor belonging to the narrow LFS tumor spectrum (eg, soft tissue sarcoma, osteosarcoma, brain tumor, premenopausal breast cancer, adrenocortical carcinoma, leukemia, and lung bronchoalveolar cancer) diagnosed before age 46 years, with at least one first- or second-degree relative with an LFS tumor (except breast cancer, if proband is affected by breast cancer) before age 56 years or with multiple tumors; or a proband with multiple tumors, two of which belong to the narrow LFS tumor spectrum (except multiple primary breast cancers) and the first of which occurred before age 46 years; or a patient with adrenocortical carcinoma or a choroid plexus carcinoma or a patient diagnosed with breast cancer before age 36 years without *BRCA1* or *BRCA2* mutation, irrespective of family history.

Gonzalez et al[1] indicated that patients with breast cancer younger than age 30 years with no first- or second-degree relative with cancer have a 7% chance of having a *TP53* mutation. Therefore, we would like to highlight our recent experience of *TP53* testing in patients with early-onset breast cancer. Our group has now performed a complete analysis of *TP53*—on the basis of sequencing the 11 exons and screening for genomic rearrangements using quantitative multiplex polymerase chain reaction of short fluorescent fragments—in 161 female patients presenting with breast cancer before age 36 years without detectable *BRCA1* or *BRCA2* mutation. In this group of patients, we identified 12 deleterious mutations and one unclassified variant (a translationally silent exonic variation) corresponding with a mutation detection rate of 7% to 8%. Among the 161 patients with breast cancer analyzed, 25 belonged to families fulfilling the familial LFS Chompret criteria; we identified a *TP53* mutation in four (16%) of the 25. Eight patients without familial history suggestive of LFS presented not only with breast cancer but also with other LFS-related tumors; three (38%) of the eight were found to have a *TP53* mutation. The 128 remaining patients were selected for *TP53* analysis only on the basis of the development of breast cancer before age 36 years and absence of *BRCA1* or *BRCA2* mutation; a *TP53* mutation or unclassified variant was detected in only five (4%) of the 128.

**Table 1.** 2009 Chompret Criteria for Germline *TP53* Mutation Screening

| | Criterion |
|---|---|
| I. | Proband with tumor belonging to LFS tumor spectrum (eg, soft tissue sarcoma, osteosarcoma, brain tumor, premenopausal breast cancer, adrenocortical carcinoma, leukemia, lung bronchoalveolar cancer) before age 46 years AND at least one first- or second-degree relative with LFS tumor (except breast cancer if proband has breast cancer) before age 56 years or with multiple tumors; OR |
| II. | Proband with multiple tumors (except multiple breast tumors), two of which belong to LFS tumor spectrum and first of which occurred before age 46 years; OR |
| III. | Patient with adrenocortical carcinoma or choroid plexus tumor, irrespective of family history |

Abbreviation: LFS, Li Fraumeni syndrome.

We conclude that the *TP53* mutation detection rate in patients with early-onset breast cancer without familial history of cancer or multiple primary tumors is less than 5%. Considering this low mutation detection rate with regard to the psychologic distress induced by *TP53* genetic testing, we think that avoidance of *TP53* testing in patients with early-onset breast cancer without familial history of cancer or multiple primary tumors would be appropriate. On the basis of our experience in *TP53* testing and the study by Gonzalez et al,[1] highlighting in particular the predictive value of choroid plexus tumors, we propose a 2009 version of the Chompret criteria to help clinicians to recognize Li Fraumeni syndrome (Table 1).

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## ACKNOWLEDGMENT

We thank the members of the Groupe Génétique et Cancer for fruitful discussion and Mario Tosi for critical review of the manuscript. This work was supported by the French National Cancer Institute.

## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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DOI: 10.1200/JCO.2009.22.7967; published online ahead of print at www.jco.org on August 3, 2009