

**Supplement to *Dagogo-Jack et al.***

**Clinical Utility of Rapid EGFR Genotyping in Advanced Lung Cancer**

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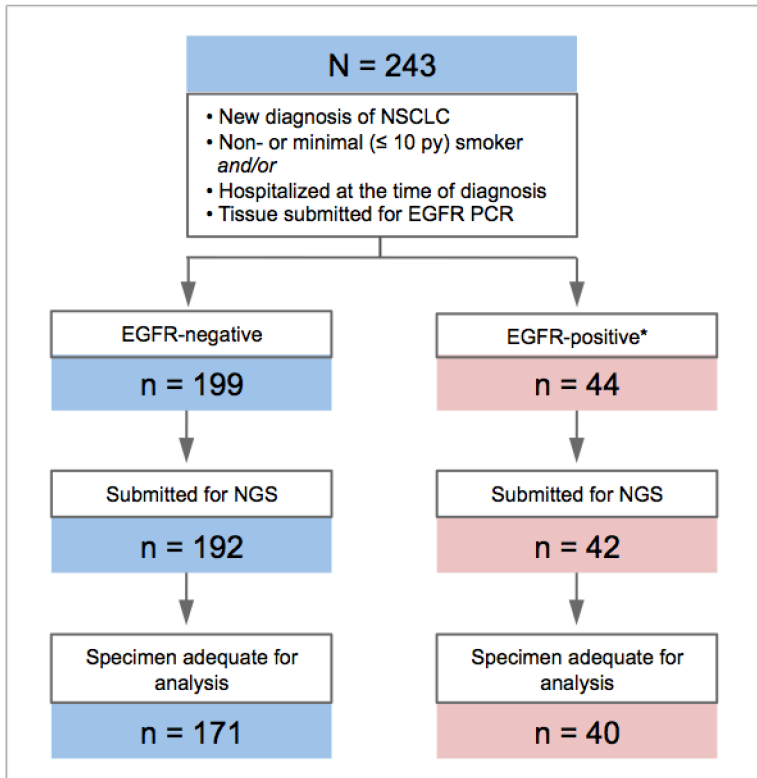
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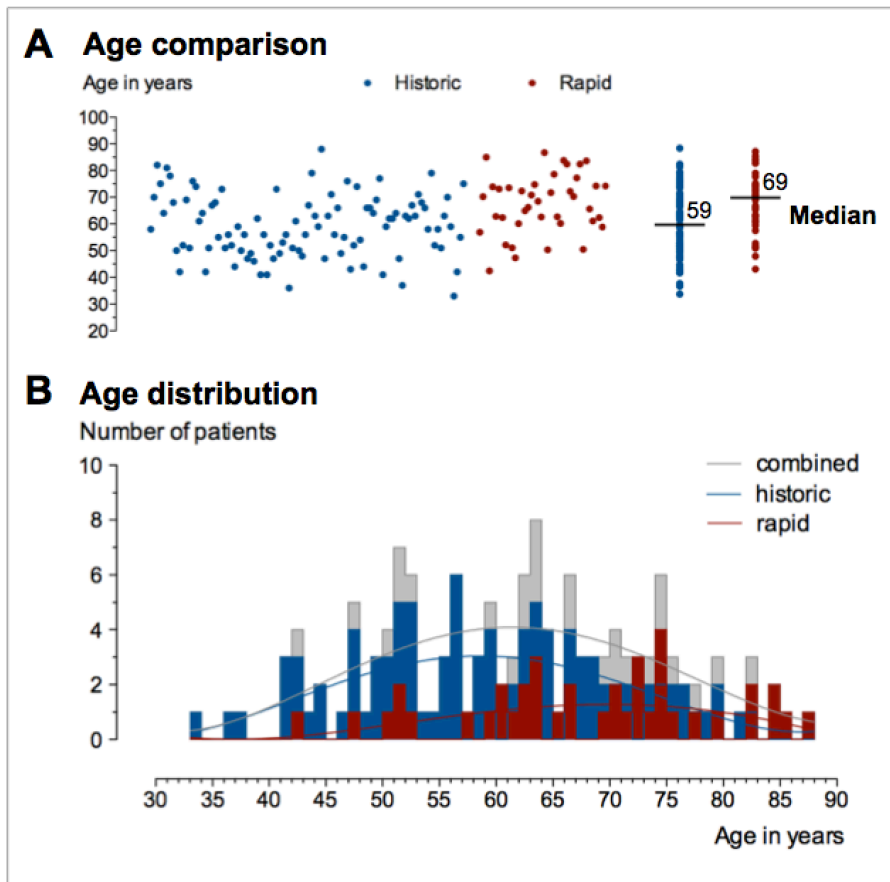
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**Supplemental Figure 1.** Inclusion criteria, patient numbers, and EGFR results

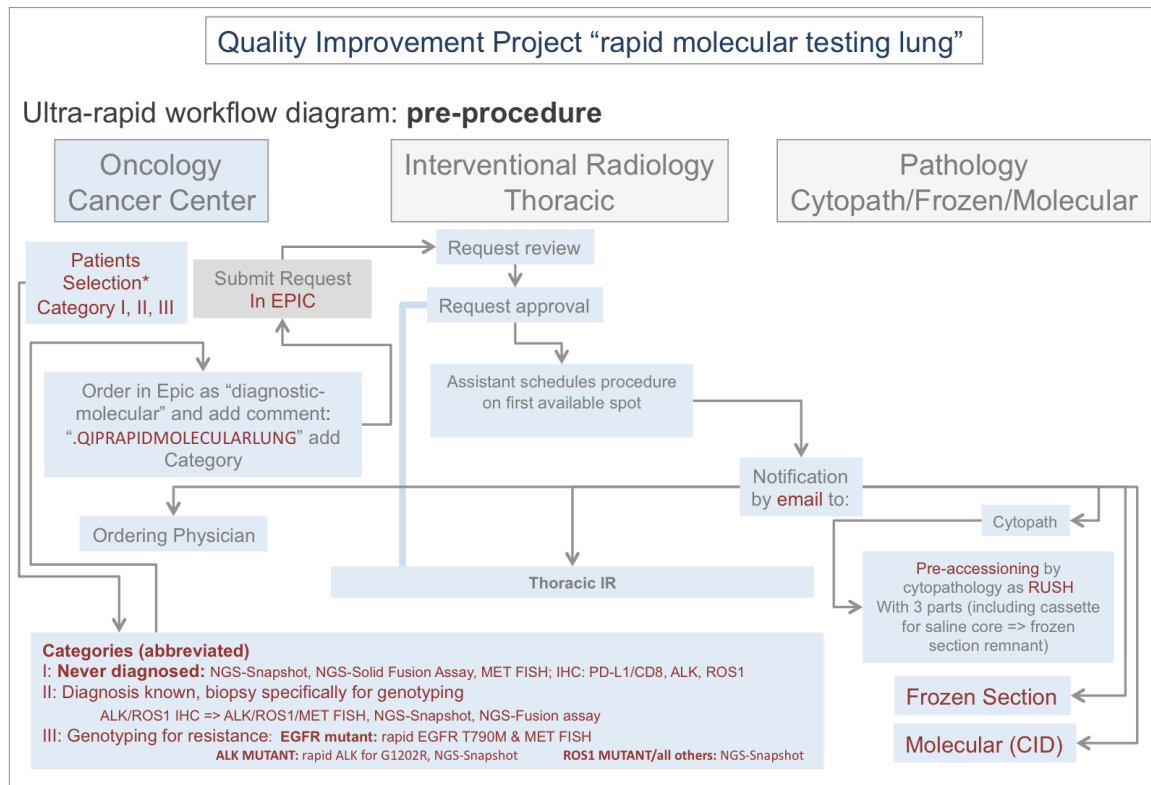


*\*Includes one patient with a non-canonical EGFR exon19del*

**Supplemental Figure 2.** Age comparison and distribution between cohorts.



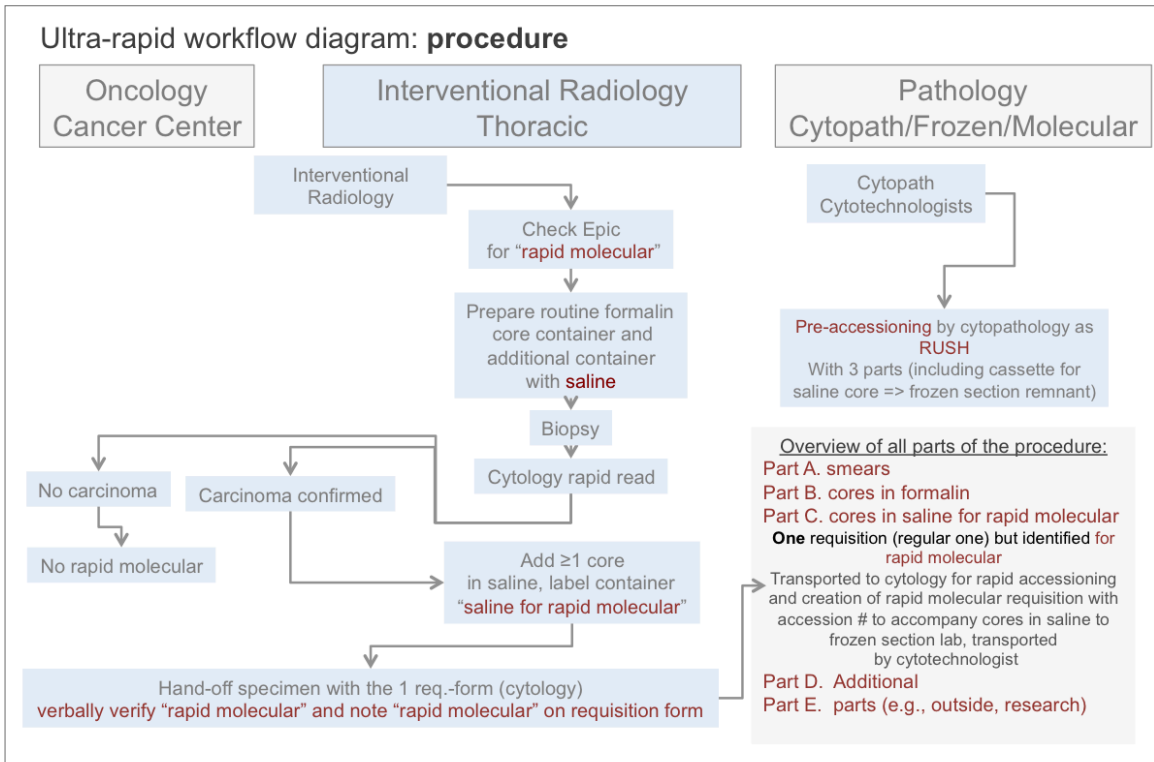
### Supplemental Figure 3. Ultra-rapid workflow: pre-procedure



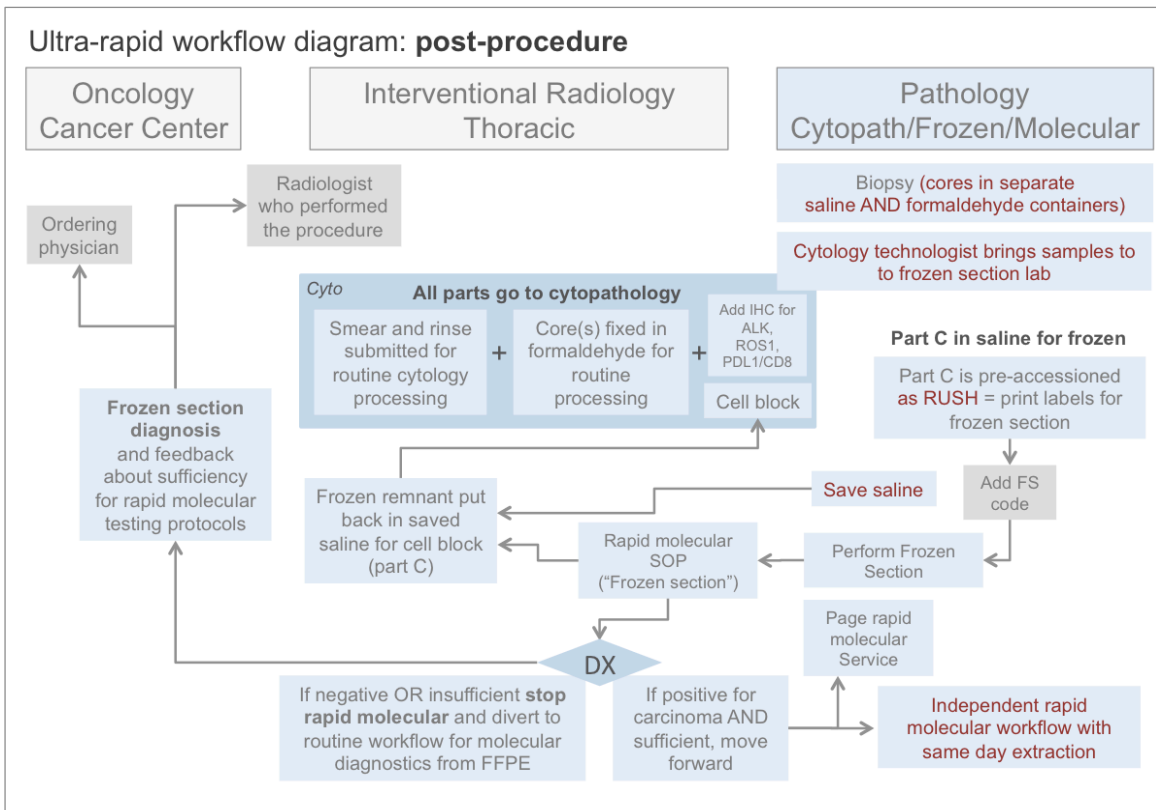
#### \* Clarification of patient selection in our practice

At our institution, we have an inpatient oncology consult service that is run by an oncology nurse practitioner and staffed by disease center-specific medical oncologists. When patients are admitted to the general medicine service and there is a suspicion for lung cancer, the oncology service is contacted to provide guidance regarding optimal biopsy sites and recommended diagnostic tests. In our practice, thoracic oncologists exclusively initiate the illustrated rapid lung cancer-testing pathway; however, the execution of the rapid workflow is very much multidisciplinary (see also main Figure 1). Specifically, triggering the pathway and coordinating the biopsy/specimen collection involves communication between thoracic oncology, molecular pathology, general surgical pathology, and the interventionalist performing the procedure (either interventional pulmonology, thoracic surgery, or interventional radiology). We believe that limiting the providers who can initiate the pathway makes the best use of resources and ensures selection of appropriate patients.

**Supplemental Figure 4. Ultra-rapid workflow: procedure**



**Supplemental Figure 5. Ultra-rapid workflow: post-procedure**



**Supplemental Table 1.** Clinicopathological features of EGFR-mutant patients in the rapid and historic cohorts

| Clinical Characteristics               | Rapid Group<br>(n = 44)* | Historical Group<br>(n = 121) | P value      |
|--|--------------------------|-------------------------------|--------------|
| <b>Age at Diagnosis (years)</b>        |                          |                               |              |
| Average                                | 67.2                     | 58.3                          | <0.001       |
| Median                                 | 68                       | 58                            |              |
| Range                                  | 42–86                    | 26–88                         |              |
| <b>Sex—number (%)</b>                  |                          |                               |              |
| Male                                   | 12 (27)                  | 41 (34)                       | 0.457        |
| Female                                 | 32 (73)                  | 80 (66)                       |              |
| <b>Smoking History—number (%)</b>      |                          |                               |              |
| Never                                  | 32 (73)                  | 76 (63)                       | 0.569        |
| Light (≤10 pack years)                 | 5 (11)                   | 13 (11)                       |              |
| Heavy (> 10 pack years)                | 6 (14)                   | 27 (22)                       |              |
| Unknown                                | 1 (2)                    | 5 (4)                         |              |
| <b>Histology—number (%)</b>            |                          |                               |              |
| Adenocarcinoma                         | 44 (100)                 | 117 (97)                      | 0.22         |
| Squamous                               | 0 (0)                    | 2 (1.5)                       |              |
| Poorly Differentiated Carcinoma        | 0 (0)                    | 2 (1.5)                       |              |
| Other                                  | 0 (0)                    | 0 (0)                         |              |
| <b>ECOG**—number (%)</b>               |                          |                               |              |
| 0 or 1                                 | 37 (76)                  | 56 (46)                       | 0.56         |
| ≥ 2                                    | 7 (10)                   | 7 (6)                         |              |
| Unknown                                | 0 (0)                    | 58 (48)                       |              |
| <b>Brain Metastases***—number (%)</b>  |                          |                               |              |
| Present                                | 25 (57)                  | 47 (39)                       | <b>0.05</b>  |
| Absent                                 | 19 (43)                  | 74 (61)                       |              |
| <b>EGFR TKI Line of Therapy—no (%)</b> |                          |                               |              |
| 1st                                    | 40 (91)                  | 98 (81)                       | <b>0.006</b> |
| Other                                  | 2 (4.5)                  | 23 (19)                       |              |
| Unknown (Lost to Follow-Up)            | 2 (4.5)                  | 0 (0)                         |              |

\* Includes the false-negative EGFR+ patient. As a result, the calculations are slightly different than those described in the manuscript. \*\*As documented by the treating physician at diagnosis; \*\*\*At diagnosis; The patient in the rapid cohort with an *EGFR* exon 19 deletion that did not involve the LREA segment is not included in this analysis. P values from t-test, Fisher's exact test for dichotomous variables, or  $\chi^2$  test.

**Supplemental Table 2.** Probabilities of therapeutically actionable variants pre- and post rapid EGFR testing

| Subsets          | pre-rapid probabilities |               |            |              | post-rapid probabilities<br>rapid EGFR negative |            |              |                    |
|------------------|-------------------------|---------------|------------|--------------|---|------------|--------------|--------------------|
|                  | N=                      | N=243         | actionable |              | N=200   | actionable |              | delta by subset    |
|                  |                         | %             | n=         | %            | %   | n=         | %            |                    |
| EGFR (rapid)     | 43                      | 17.60%        |            |              |   |            |              |                    |
| EGFR (remaining) | 15                      | 6.17          | 1          | 0.41         | 7.5   | 1          | 0.50         | 0.09               |
| ALK              | 11                      | 4.53          | 11         | 4.53         | 5.5   | 11         | 5.50         | 0.97               |
| ROS1             | 6                       | 2.47          | 6          | 2.47         | 3   | 6          | 3.00         | 0.53               |
| MET              | 15                      | 6.17          | 15         | 6.17         | 7.5   | 15         | 7.50         | 1.33               |
| ERBB2            | 8                       | 3.29          | 8          | 3.29         | 4   | 8          | 4.00         | 0.71               |
| RET              | 2                       | 0.82          | 2          | 0.82         | 1   | 2          | 1.00         | 0.18               |
| BRAF             | 10                      | 4.12          | 10         | 4.12         | 5   | 10         | 5.00         | 0.88               |
| PIK3CA           | 6                       | 2.47          |            |              | 3   |            |              |                    |
| KRAS             | 60                      | 24.69         |            |              | 30  |            |              |                    |
| other            | 33                      | 13.58         |            |              | 16.5  |            |              |                    |
| not detected     | 15                      | 6.17          |            |              | 7.5   |            |              |                    |
| NGS failed       | 19                      | 7.82          |            |              | 9.5   |            |              |                    |
| rapid EGFR       |                         | 17.60%        |            |              |   |            |              | delta pre vs. post |
| added NGS        |                         | 21.81%        |            | <b>21.81</b> | <b>added NGS if rapid=neg.</b>                  |            | <b>26.50</b> | <b>4.69</b>        |
| <b>total</b>     |                         | <b>39.41%</b> |            |              |   |            |              |                    |



**Supplemental Table 3. Involved sites and presenting symptoms of patients in the ultra-rapid cohort**

| <b>Patient</b> | <b>Sites of Disease at Diagnosis*</b> | <b>Symptoms at Presentation</b>                              |
|----------------|---------------------------------------|--|
| 1              | axillary node, brain                  | chest pain   |
| 2              | left ventricle                        | cardioembolic stroke with vision loss, chest pain            |
| 3              | brain, multiple lung nodules          | cough  |
| 4              | bone                                  | bone pain  |
| 5              | brain, liver                          | left arm weakness, gait instability                          |
| 6              | bone, brain, lung                     | difficulty swallowing, hearing loss, gait instability, cough |
| 7              | bone, supraclavicular nodes           | bone pain  |
| 8              | brain, choroid, liver, pleura         | vision loss  |

\*Excludes primary lung mass and thoracic nodes