We identified amplification of RICTOR, a key component of the mTOR complex 2 (mTORC2), as the sole actionable genomic alteration in an 18-year-old never-smoker with lung adenocarcinoma. Amplification of RICTOR occurs in 13% of lung cancers (1,016 cases) in The Cancer Genome Atlas and at a similar frequency in an independent cohort of 1,070 patients identified by genomic profiling. In the latter series, 11% of cases harbored RICTOR amplification as the only relevant genomic alteration. Its oncogenic roles were suggested by decreased lung cancer cell growth both in vitro and in vivo with RICTOR ablation, and the transforming capacity of RICTOR in a Ba/F3-cell system. The mTORC1/2 inhibitors were significantly more active against RICTOR-amplified lung cancer cells as compared with other agents targeting the PI3K–AKT–mTOR pathway. Moreover, an association between RICTOR amplification and sensitivities to mTORC1/2 inhibitors was observed. The index patient has been treated with mTORC1/2 inhibitors that led to tumor stabilization for more than 18 months.

SIGNIFICANCE: RICTOR amplification may define a novel and unique molecular subset of patients with lung cancer who may benefit from treatment with mTORC1/2 inhibitors.

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INTRODUCTION

The advent of targeted therapeutics against oncogenic genomic alterations has revolutionized the treatment paradigm in subgroups of patients with lung cancer. However, targetable genomic alterations have not been identified in nearly half of lung adenocarcinomas (1). We evaluated an 18-year-old male never-smoker with lung adenocarcinoma for possible targeted therapy. The only genomic alteration identified by a hybridization capture–based next-generation sequencing assay (FoundationOne) was amplification of RICTOR.

RICTOR, the defining component of the mTOR complex 2 (mTORC2; ref. 2), is the upstream kinase of several AGC kinase family members, including AKT, SGK, S6K mutants, and several PKC isoforms (3, 4). Activation of RICTOR–mTORC2 modifies actin organization and promotes cell proliferation and survival. The less well-characterized mTOR-independent functions of RICTOR regulate cell morphology, migration, and protein degradation (3, 5). In the context of...
these diverse functions, mTORC2 has critical oncogenic roles in regulating cancer cell migration, invasion, and metastasis in gliomas and in breast, ovarian, prostate, and colorectal cancers (6–8). Specifically, PTEN-induced prostatic oncogenesis is dependent on RICTOR dosage (8). Recently, the overexpression of RICTOR was demonstrated to be a direct target of mTORC2–RICTOR and two downstream targets of mTORC1 complex, p4EBP1 and pS6RP. Given the complex interplay between mTORC1 and mTORC2, activation of AKT secondary to RICTOR amplification may have induced “cross-talk” and subsequently activated mTORC1 signaling (Supplementary Fig. S1B).

Given activation of both mTORC1 and mTORC2 signaling, the index patient was treated on a phase I clinical trial with a dual mTORC1/2 inhibitor, MLN0128, on a phase I trial in February 2015. Restaging imaging with CT of the chest/abdomen after 6 cycles revealed stable disease, and he continues to receive treatment with this agent.

The Frequency of RICTOR Amplification in Lung Cancer

To evaluate the relevance of our observations to the broader population of cancer patients, we first reviewed The Cancer Genome Atlas (TCGA) database for RICTOR alteration in all types of cancer (Supplementary Fig. S2) and found that RICTOR is amplified in around 13% (132/1,016) of patients with lung cancers, including 10.3% in lung adenocarcinoma (53/515) and 15.8% (79/501) in squamous cell carcinoma (see TCGA Data Portal; refs. 10–13). Lung cancer appears to be one of the tumors with the highest frequency of RICTOR amplification.

Focal RICTOR amplification was identified in 8% of 1,070 lung cancer cases assayed at Foundation Medicine (85/1,070), including 14.6% in small cell lung cancer (7/48), 8.7% in large cell neuroendocrine carcinoma (2/23), 8.4% in adenocarcinoma (61/724), and 7.4% in squamous cell carcinoma (8/108). Interestingly, RICTOR amplification was the sole potentially actionable target in the tested gene panel in 11% of 85 cases. The median age for these patients with RICTOR amplification as the only actionable alteration is 64 years old, including 58% female (49/85) and 42% male (36/85). One third of the cases with RICTOR amplification (29/85) had alterations in other genes within the PI3K–AKT–mTOR pathway. In addition, 26% (22/85) and 14% (12/85) of these patients had alterations in EGFR and KRAS as an additional alteration in lung adenocarcinomas (Fig. 1B; Supplementary Fig. S3A and S3B). Nonfocal RICTOR amplifications were detected in 21 cases, and they were excluded from the analysis.

The Effects of RICTOR Knockdown on RICTOR-Amplified and RICTOR-Nonamplified Lung Cancer Cells

We screened a tissue microarray of lung cancer cell lines for RICTOR amplification using the FISH assay. The majority of cell lines had normal copy numbers of RICTOR with a ratio of RICTOR/control around 1, but 3 of 27 non–small cell lung cancer (NSCLC) cell lines, including H23, H1734, and H1703, were found to have a ratio of RICTOR/control of 2, indicating amplification of RICTOR (Fig. 2A). Of note, in addition to RICTOR amplification, H23 also harbors a KRAS mutation, whereas H1703 has a PDGFR amplification.

The effects of siRNA-mediated RICTOR knockdown in RICTOR-amplified H23 and H1703 cells were next examined. Both siRNAs diminished RICTOR expression, and the decrease in both AKT and p4EBP1 phosphorylation and colony formation was consistent with a functional effect of this intervention (Fig. 2A). Similarly, inducible shRNA RICTOR knockdown was also associated with significantly reduced proliferation of both H23 and H1703 cells (Fig. 2B and C). We next examined the role of RICTOR in lung tumor growth
Figure 1. A, timeline of diagnosis, treatment, and responses of the index patient with RICTOR amplification. Inset, Western blot: CC-223 therapy was associated with modest inhibition of pAKT S473 and p4EBP1 in patient’s blood cells (PBMC). RICTOR amplification, mTORC1/2 inhibitors, and their responses shown in red. Carbo, carboplatin; Dx, diagnosis; dz, disease; ImmunoRx, immunotherapy; NGS, next-generation sequencing; pem, pemetrexed; POD, progression of disease; PR, partial response.

B, tile plot showing the gene alterations in each individual with RICTOR-amplified tumors, focusing on the commonly assessed genomic alterations in lung cancer (RTK/RAS/RAF) and PI3K/AKT/mTOR alterations. For the full list, please refer to Supplementary Fig. S3A and S3B. Note: The case of the index patient was sequenced in 2012 using the FoundationOne 182 gene panel, and all 85 RICTOR-amplified cases presented in B used the FoundationOne 236 gene panel. Thus, the index patient is not included in the 85-case amplified series.
Figure 2. The effects of genetic knockdown of RICTOR and pharmacologic inhibition on RICTOR-amplified lung cancer cells. A, FISH in lung cancer cell lines: both H23 and H1703 cells have a ratio of RICTOR/control of 2, and thus are RICTOR amplified. Western blotting and colony formation assays: the effects of transient siRNA-mediated RICTOR knockdown on RICTOR-amplified H23 cells and H1703 cells. *, P < 0.05. B, Western blot: the effects of inducible shRNA-mediated RICTOR knockdown on RICTOR-amplified H23 cells and H1703 cells. The addition of doxycycline led to RICTOR knockdown in cells. C, colony formation assay: the addition of doxycycline led to RICTOR knockdown and was associated with decreased colony formation. *, P < 0.05. D, xenograft mouse models: the effects of inducible shRNA-mediated RICTOR knockdown on H23 cells and H1703 xenografts. *, P < 0.05. E, the effects of PI3K/AKT/mTOR inhibitors on RICTOR-amplified H23 cells. Among all the examined agents targeting the PI3K-AKT-mTOR pathways, BEZ235 (dual PI3K/mTOR inhibitor) and AZD2014 (dual mTORC1/2 inhibitor) were the most potent and showed similar inhibition of pmTOR, pAKT S473, and pS6.
in vivo using murine xenografts. As shown in Fig. 2D, inducible RICTOR knockdown significantly reduced H1703 xenograft tumor growth. Taken together, genetic ablation of RICTOR is associated with growth inhibition of RICTOR-amplified lung cancer, consistent with RICTOR’s role as an oncogenic driver.

The in vitro potency of inhibitors targeting different components of the PI3K–AKT–mTOR pathways, including BEZ235 (dual PI3K/mTOR inhibitor), AZD2014 (dual mTORC1/2 inhibitor), RAD001 (everolimus, a rapamycin analogue and mTORC1 inhibitor), MK2206 (AKT inhibitor), and LY294002 (PI3K inhibitor), as well as erlotinib (EGFR tyrosine kinase inhibitor), was determined. Among all the examined agents, BEZ235 and AZD2014 were the most potent in RICTOR-amplified H23 cells in a concentration-dependent manner. As expected for dual mTORC1/2 inhibitors, both agents decreased phosphorylation of S6RP, AKT, and mTOR (Fig. 2E). In contrast, RAD001 inhibited only pS6 and slightly increased pAKT<sup>S473</sup>, suggestive of a feedback effect between mTORC1 and mTORC2. Analogous results were observed in H1703, another RICTOR-amplified lung cancer cell line (data not shown).

We also examined the role of RICTOR in lung cancer cells that lack RICTOR amplification but contain other molecular abnormalities. We found that RICTOR knockdown also reduced colony formation in NSCLC cell lines that lack RICTOR amplification, such as A549 (KRAS mutated) and HCC827 (EGFR mutated; Fig. 3A and B). Furthermore, when RICTOR expression was continuously decreased with doxycycline treatment of tumor-bearing mice for around 4 weeks, the growth of A549 and HCC827 lung tumor xenografts was markedly reduced by 75% and 66% (P < 0.05; Fig. 3C). Taken together, the results indicate that RICTOR plays important roles in regulating cell survival and proliferation in RICTOR-expressing lung cancer cells. A potential negative implication of growth inhibition in nonamplified tumors is the possible toxicity to normal cells. However, clinical studies have shown that mTORC1/2 inhibitors, such as CC-223 and MLN0128, which block RICTOR–mTORC2 signaling, are generally well tolerated in unselected patients with cancer (14). Thus, RICTOR-targeted therapy may potentially be a novel therapeutic strategy for both RICTOR-amplified lung cancers and RICTOR-expressing but nonamplified tumors.

Association between RICTOR Amplification and Sensitivities to mTORC1/2 Inhibitors in a Panel of Lung Cancer Cell Lines

Ideally, an association between the sensitivity of a pure RICTOR inhibitor and RICTOR levels in cells with the same genetic background would best support our hypothesis. However, a pure RICTOR or mTORC2 inhibitor has not yet been reported. Thus, we tested dual mTORC1/2 inhibitors that block both mTORC1 and mTORC2 signaling. A trend associating RICTOR amplification with sensitivity to mTORC1/2 inhibitors, such as MLN0128 and AZD2014, was notable (Table 1; data for AZD2014 not shown). The IC<sub>50</sub> values for RICTOR-amplified H23 and H1703 cells were quite low, around 10 nmol/L. Furthermore, silencing of RICTOR rendered RICTOR-amplified H23 or H1703 cells markedly more resistant to mTORC1/2 inhibitors, likely by eliminating the relevant target, RICTOR amplification, in those cells. In contrast, the IC<sub>50</sub> of MLN0128 did not change as much in RICTOR-nonamplified cells, such as A549, HCC827, and PC9 after RICTOR ablation, indicating that RICTOR may not be as relevant a target for mTORC1/2 inhibitors in those cells. Of note, the potential sensitivity of the cells to mTORC1 inhibition may complicate or mask the association between RICTOR amplification and the effects of the dual mTORC1/2 inhibitors because RICTOR is a key component of mTORC2 but not mTORC1. Taken together, there is an association between RICTOR amplification and sensitivities to mTORC1/2 inhibitors in NSCLC cells.

The Ability of RICTOR Induction to Transform Ba/F3 Cells to Growth Factor Independence and Its Association with Sensitivity to mTORC1/2 Inhibitors

The previously tested lung cancer cell lines have multiple different genetic alterations. To examine the effects of RICTOR amplification in isolation, we examined Ba/F3 cells that were transfected with a construct to inducibly overexpress RICTOR in the presence of doxycycline (Fig. 3D). These cells, which are normally dependent on IL3 for proliferation, were transformed to IL3 independence by the upregulation of RICTOR (Fig. 3E), supporting the role of RICTOR as an oncogene.

Furthermore, in isogenic Ba/F3–RICTOR cells in which the RICTOR level can be regulated by the addition of doxycycline, the IC<sub>50</sub> of two structurally different mTORC1/2 inhibitors (MLN0128 and AZD2014) decreased with higher RICTOR levels (Fig. 3F, P < 0.05). This indicates that RICTOR amplification is associated with improved sensitivity to mTORC1/2 inhibitors. Thus, the results are consistent with RICTOR amplification as a potential oncogenic driver that can also sensitize Ba/F3 cells to mTORC1/2 inhibitors.

DISCUSSION

In the present study, we identified RICTOR amplification as the sole actionable genomic alteration in an 18-year-old patient with lung cancer by a highly sensitive hybrid capture-based next-generation sequencing strategy (15). Reviews of the TCGA database and an independent series revealed that RICTOR amplification occurs in 8% to 13% of patients with lung cancer. In the second dataset, we found that it occurs either as the sole potentially actionable gene target (11%) or with other genomic alterations. The RICTOR ablation–associated decrease in cancer cell growth in RICTOR-amplified NSCLC cells and the transforming capacity of RICTOR-dependent Ba/F3 cells suggest that RICTOR regulates cancer cell survival and proliferation, consistent with a role as an oncogenic driver in some settings.

Dual mTORC1/2 blockers were found to be the most active agents against RICTOR-amplified lung cancer cells among the inhibitors of PI3K–AKT–mTOR tested. Consistent with this in vitro finding, our index patient had tumor stabilization for more than 18 months from treatment with dual mTORC1/2 inhibitors, such as previously CC-223 and currently MLN0128. Both agents are orally available, ATP-competitive inhibitors of mTOR kinase that block both mTORC1 and mTORC2 signaling and are in clinical development. This was a striking result when compared with the typical outcome in a heavily pretreated patient with NSCLC that has progressed on multiple regimens previously (16).
**RICTOR Amplification in Lung Cancer**

**Figure 3.**

A, FISH in lung cancer cell lines revealed that neither A549 nor HCC827 cells were RICTOR amplified. B, Western blotting and clonogenic assays: the effects of siRNA-mediated RICTOR knockdown on RICTOR-expressing but nonamplified A549 and HCC827 cells. *, *P* < 0.05. 

C, the in vivo effects of RICTOR knockdown in RICTOR-expressing but nonamplified A549 and HCC827 xenograft mouse models. *, *P* < 0.05. 

D, Western blot: RICTOR expression in parental Ba/F3 cells and inducible Ba/F3–RICTOR cells. Ba/F3–RICTOR were inducible Ba/F3 cells with RICTOR overexpression in the presence of doxycycline. IL3 was withdrawn for 2 days for the parental Ba/F3 cells and was not added for 1 month for the rest. Of note, although the inducible Ba/F3–RICTOR system had some “leakage” of RICTOR expression in the absence of doxycycline, the addition of doxycycline caused higher IL3-independent RICTOR expression and cell survival. 

E, relative viable cells after withdrawal of IL3. 

F, modulation of IC50 of two structurally different mTORC1/2 inhibitors, MLN0128 and AZD2014, when RICTOR was upregulated by the addition of doxycycline in Ba/F3–RICTOR cells. *, *P* < 0.05 when comparing IC50 of Ba/F3–RICTOR cells in the absence of doxycycline versus IC50 in the presence of doxycycline. It appears that higher levels of RICTOR rendered Ba/F3–RICTOR cells more sensitive to mTORC1/2 inhibitors.
In contrast, previous studies have shown limited clinical benefit from mTORC1/2 inhibitors in unselected patients with lung cancer (17). Our findings suggest that stratifying patients by genomic profiles, specifically RICTOR amplification, for future incarnations of these trials may lead to better patient selection. Results were just published of a phase I trial on CC-223 in patients with advanced solid tumors (18). Among 28 patients (2 with NSCLC) who were enrolled and who received CC-223, the best responses were 1 partial response in a patient with breast cancer (response duration, 220 days) and 8 subjects with stable disease with response duration ranging from 36 to 168 days. Our index patient had stable disease for 12 months (±365 days) on CC-223, which represents a 66% increase over the best results observed with the patient who had a partial response of 220 days. Therefore, he seems to be an outlier in the context of the available clinical data with CC-223. Furthermore, his disease rapidly progressed after 3 months of combined immunotherapy, but was stabilized again with another dual mTORC1/2 inhibitor, MLN0128. Taken together, our patient has had much longer disease control with mTORC1/2 inhibitors in comparison with available published data.

There are several potential reasons for the index patient’s not having had a more robust response. First, the dose of mTORC1/2 inhibitors that he received may not have been sufficient to adequately inhibit the targets in the tumor. Second, because CC-223 and MLN0128 are inhibitors of mTORC1/2 but not specific RICTOR inhibitors, they will not block mTORC2-independent RICTOR signaling. It is also possible that the type of tumor response to targeted therapies against amplification of oncogenes may differ from targeted therapies against driver gene mutations and translocations. ERBB2/HER2 amplification-targeted therapy, including trastuzumab, is so far the only FDA-approved treatment targeting gene amplification. Unlike the impressive responses associated with specific kinase inhibitors against EGFR and other driving mutations, single-agent trastuzumab therapy was associated with an overall response rate of only 15% and duration of response of 9.1 months in the second-/third-line monotherapy trial conducted in patients with HER2-positive metastatic breast cancer (19). On the other hand, targeted therapy against ERBB2 amplification has transformed the field of breast cancer management, providing further impetus to investigate a potential paradigm for the use of RICTOR-targeted therapy for RICTOR-amplified lung cancer.

In addition to its role in NSCLC, a relatively high degree of RICTOR amplification was also observed in small cell lung cancer (14.6%), which is similar to the previously reported frequency (20, 21). The mTORC1 inhibitors, such as everolimus (RAD001; ref. 22), and inhibitors targeting both mTORC1 and mTORC2 have been tested in small cell lung cancer with very limited responses in unselected patients (22). Thus, future studies will be needed to investigate whether patients with small cell lung cancer can be stratified based on RICTOR amplification to derive clinical benefits from mTORC1/2 inhibitors.

In summary, the initial clinical data presented here suggest that patients with RICTOR-amplified NSCLC may benefit from treatment with dual mTORC1/2 inhibitors, especially in cases where RICTOR is the sole oncogenic driver. Our clinical and laboratory observations provide the rationale for (re)evaluating dual mTORC1/2 inhibitors as a potential therapy for patients with lung cancer, as stratified by genomic profiling to assess both RICTOR amplification and the remainder of the genomic background, as our index patient may have benefitted from the absence of other known oncogenic drivers in responding to mTORC1-targeted therapy. A first key step in that direction will be to identify specific RICTOR inhibitors, and for that purpose, a high-throughput drug screen is currently under way.
**METHODS**

**Cell Lines and Material**

The H23, H1703, A549, HCC827, H157, H460, H2228, H3122, and H322 NSCLC cell lines were obtained from the American Type Tissue Collection and were grown in RPMI 1640 supplemented with 10% FBS and 1× antibiotic/antimycotic (Invitrogen). Among them, cell lines H23, HCC827, H1703, and A549 were tested and authenticated by short tandem repeat profiling in August 2014 and 2015, and the rest were not authenticated. PC9 cells were a gift from Dr. Susumu Kobayashi (Harvard Medical School, Boston, MA). Ba/F3 cells were obtained from G. Gilliland (Brigham and Women’s Hospital, Boston, MA). RICTOR-dependent Ba/F3 cells were developed by transfecting Ba/F3 cells with a doxycycline-inducible plasmid for the overexpression of wild-type RICTOR in the presence of doxycycline (RICTOR-pTetOne, modified from Tet-One Systems, Clontech Laboratories, Inc., and generated by GENEWIZ, Inc.). BEZ235, AZD2014, RAD001 (everolimus), erlotinib, MK2206, and LJ294002 were obtained from Selleck Chemicals; cisplatin was obtained from Sigma-Aldrich.

**Immunoblotting and Antibodies**

Western blot analysis was performed as described (23). Antibodies against RICTOR, phospho-mTOR, phospho-EGFR, phospho- AKT(p70), phospho-S6RP (S235/236), phospho-4EBP1 (T37/46), phospho-ERK1/2, tubulin, and GAPDH were from Cell Signaling Technology. The RICTOR antibody used in IHC was from Bethyl Laboratories.

**PBMC Isolation and Analysis of Patient’s Specimen**

The patient’s PBMCs were isolated by Ficoll density gradient centrifugation (24). The collection and analysis of this patient’s sample were carried out in accordance with the Declaration of Helsinki, and the protocols were approved by the Institutional Review Board of Albert Einstein College of Medicine. Informed consent for genomic analysis was obtained from the patient.

**IHC**

IHC was performed as previously described (23) with formalin-fixed primary lung tumor tissue slides. RICTOR antibody was used at a dilution of 1:5,000 (optimal dilution for overnight incubation) at room temperature.

**Tissue Microarray of Lung Cancer Cell Lines**

The formalin-fixed, paraffin-embedded tissue microarray of lung cancer cell lines includes 27 NSCLC cell lines.

**Clonogenic Survival Assay**

As previously described (25), logarithmically growing cells were plated in triplicate. All drugs were administered for 5 days, after which colonies were fixed with 70% EtOH and stained with 0.5% crystal violet. Surviving colonies were defined as colonies containing > 50 cells.

**MTS Cell Growth Assay**

Lung cancer cells were seeded at a density of 3,000 cells (or 1,500 cells for siRNA and shRNA experiments) per well in 96-well plates (26). All drugs were left on the cells for 3 days. Viable cell numbers were determined using the MTS assay kit according to the manufacturer’s protocol (Promega).

**siRNA Knockdown**

Knockdown of RICTOR was performed using siRNAs (Dharmacon RNAi Technologies, Thermo). SiGENOME nontargeting siRNA pools served as negative controls.

**Inducible shRNA Knockdown**

The Thermo Scientific Open Biosystems Expression Arrest TRIPZ Lentiviral shRNAmir was used per the manufacturer’s manual (TRIPZ Human RICTOR shRNA, Thermo Fisher Scientific). Pooled NSCLC cells with inducible shRNA–RICTOR were utilized within a month following transduction.

**FISH**

FISH for the detection of copy-number variations mapping to the RICTOR locus (chr5:38,938,023-39,074,510) was performed using the following locus-specific probes: BAC clones RP11-315A2 (chr5:38,840,944-38,995,845) and RP11-44D11 (chr5:39,184,412-39,386,845) both mapping to chr5p13.1 and spanning 545,902 bp across the RICTOR locus, and a control reference clone RP11-204D12 (chr5:95,677,452-95,844,184) mapping distal to the RICTOR region of interest (chr5q13.1 and 56Mb distal the RICTOR-specific clones). FISH was performed as previously described (27). Similar to HER2 amplification, RICTOR amplification is defined as a ratio of RICTOR/control ≥ 2.

**Xenograft Mouse Studies**

SCID mice (The Jackson Laboratory, female, 9–10 weeks old) were inoculated subcutaneously with 5 × 10^6 NSCLC cells. After 2 days, mice were divided into a vehicle control (water) group and a doxycycline group, with 5 mice in each group. Doxycycline was administered by oral gavage: 100 mg/kg/day (28). The same volume of water was given to the control group. A total of 20 daily doses were administered in 4 weeks. Tumors were measured with calipers twice weekly, and size was calculated as length × width^2/2. The protocol was approved by the Institutional Animal Care and Use Committee.

**Genomic Profiling of Clinical Lung Cancer Samples**

The hybridization capture-based next-generation sequencing was performed using the FoundationOne test (Foundation Medicine). The detailed laboratory and computational methods used in the FoundationOne assay have been reported (15). Data were generated from two consecutive versions of the test, targeting increasing numbers of genes. Hybridization capture baits for the RICTOR gene were identical for both versions of the test. Actionable genomic alterations are defined as those linked to FDA-approved drugs or agents under study in targeted therapy registered clinical trials. Copy-number amplifications are defined as copy number ≥ 6. Local site permissions were obtained to use clinical samples for this study.

**Statistical Analysis**

All data are expressed as mean ± SD from at least triplicate experiments. Statistical analysis was performed by one-way or two-way ANOVA as appropriate, using Statistica 6.0 (StatSoft). Differences were considered significant at P < 0.05.

**Disclosure of Potential Conflicts of Interest**

J.S. Ross reports receiving a commercial research grant from Foundation Medicine and has ownership interest (including patents) in the same. S.M. Ali has ownership interest (including patents) in Foundation Medicine. R. Yelensky has ownership interest (including patents) in Foundation Medicine. D. Lipson has ownership interest (including patents) in Foundation Medicine. P.J. Stephens has ownership interest (including patents) in Foundation Medicine. V.A. Miller has ownership interest (including patents) in Foundation Medicine. B. Piperdi is Senior Principal Scientist, Clinical Research, at Merck, and has ownership interest (including patents) in the same. No potential conflicts of interest were disclosed by the other authors.
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