Inflammmatory Myofibroblastic Tumors Harbor Multiple Potentially Actionable Kinase Fusions

Christine M. Lovly, Abha Gupta, Doron Lipson, Geoff Otto, Tina Brennan, Catherine T. Chung, Scott C. Borinstein, Jeffrey S. Ross, Philip J. Stephens, Vincent A. Miller, and Cheryl M. Coffin

ABSTRACT

Inflammmatory myofibroblastic tumor (IMT) is a neoplasm that typically occurs in children. The genetic landscape of this tumor is incompletely understood and therapeutic options are limited. Although 50% of IMTs harbor anaplastic lymphoma kinase (ALK) rearrangements, no therapeutic targets have been identified in ALK-negative tumors. We report for the first time that IMTs harbor other actionable targets, including ROS1 and PDGFRβ fusions. We detail the case of an 8-year-old boy with treatment-refractory ALK-negative IMT. Molecular tumor profiling revealed a ROS1 fusion, and he had a dramatic response to the ROS1 inhibitor crizotinib. This case prompted assessment of a larger series of IMTs. Next-generation sequencing revealed that 85% of cases evaluated harbored kinase fusions involving ALK, ROS1, or PDGFRβ. Our study represents the most comprehensive genetic analysis of IMTs to date and also provides a rationale for routine molecular profiling of these tumors to detect therapeutically actionable kinase fusions.

SIGNIFICANCE: Our study describes the most comprehensive genomics-based evaluation of IMT to date. Because there is no “standard-of-care” therapy for IMT, the identification of actionable genomic alterations, in addition to ALK, is expected to redefine management strategies for patients with this disease.

INTRODUCTION

Inflammmatory myofibroblastic tumor (IMT) is a rare mesenchymal tumor that can occur at any age, but has a predilection for children, adolescents, and young adults (1). An estimated 150 to 200 new cases are diagnosed annually in the United States (2). These soft-tissue tumors can occur at multiple anatomic sites, but most commonly involve the lung, abdomen/pelvis, and retroperitoneum. The mainstay of treatment for IMT is surgical resection; however, treatment...
options are limited for patients with unresectable and/or advanced disease.

IMTs are diagnosed pathologically using criteria established by the World Health Organization (WHO; ref. 3). These tumors are characterized histologically by a spindle myofibroblastic cell proliferation with a lymphoplasmacytic inflammatory infiltrate (4). Approximately 50% of IMTs are positive for anaplastic lymphoma kinase (ALK) expression by IHC. The most common mechanism of ALK expression and activation involves structural rearrangements in the ALK gene, leading to the formation of a chimeric fusion protein. Several ALK fusion partners have been identified retrospectively (5), as tumor sequencing is not yet the standard of care for IMTs. ALK fusions have been validated as a therapeutic target. A patient with a RANBP2–ALK-positive IMT had a partial response to the ALK tyrosine kinase inhibitor (TKI) crizotinib, whereas a patient whose IMT lacked an ALK fusion did not respond to this agent (6).

In contrast, actionable genomic alterations have not yet been described in the 50% of IMT samples that are negative for ALK by IHC. ALK-negative IMTs may be more aggressively (5), as tumor sequencing is not yet the standard of care for IMTs. ALK fusions have been validated as a therapeutic target. A patient with a RANBP2–ALK-positive IMT had a partial response to the ALK tyrosine kinase inhibitor (TKI) crizotinib, whereas a patient whose IMT lacked an ALK fusion did not respond to this agent (6).

Here, we describe the case of an 8-year-old boy with treatment-refractory ALK-negative IMT. Targeted next-generation sequencing (NGS)-based genomic profiling identified the presence of a ROS1 kinase fusion within his tumor. On the basis of this finding, he was treated with the ROS1/ALK/MET TKI, crizotinib, and experienced rapid symptomatic improvement and significant decrease in his tumor burden. This case prompted us to perform genomic analysis on a larger series of this rare tumor. Our data show for the first time that kinase fusions are found in the majority of IMTs. These data not only offer insight into this disease but also provide a rationale for routine molecular profiling to detect therapeutically actionable kinase fusions and thereby offer patients rational therapeutic strategies with existing TKIs based on the genomic profile of the tumor.

RESULTS
Case Report
A 6-year-old boy presented with a 1-year history of cough and fatigue. Imaging demonstrated the presence of a large left-sided chest mass. Biopsy of the mass revealed IMT, negative for ALK expression by standard clinical IHC and for ALK rearrangement by break-apart FISH. The tumor was deemed unresectable due to its intimate association with the pulmonary vein, aorta, and esophagus. At the time of diagnosis, his laboratory parameters were indicative of a microcytic anemia and an inflammatory state. Several treatment regimens were administered, including anti-inflammatory agents (naproxen, corticosteroids, and indomethacin) as well as cytotoxic chemotherapy (methotrexate–vinorelbine), over the course of 24 months (Supplementary Fig. S1), with no antitumor response and minimal improvement of his anemia. While he was receiving methotrexate–vinorelbine, we performed targeted NGS-based genomic profiling of his tumor using formalin-fixed and paraffin-embedded (FFPE) tissue and surprisingly detected a TFG–ROS1 fusion (Fig. 1A). ROS1 TKIs, such as crizotinib, have proven to be an effective therapeutic strategy in lung cancers harboring ROS1 kinase fusions (8, 9). Therefore, he was treated with crizotinib (250 mg), obtained through a compassionate access program, twice daily orally. He experienced grade 1 diarrhea and visual disturbance, both of which resolved with no dose reduction. Within 3 cycles of crizotinib therapy, he symptomatically felt better, with decreased cough and significantly increased energy. Imaging studies revealed, for the first time since diagnosis, a decrease in the size of his tumor mass (Fig. 1B). Notably, his hemoglobin (Hgb) and mean corpuscular volume (MCV) rapidly increased and his erythrocyte sedimentation rate (ESR) decreased (Fig. 1C and Supplementary Table S1). He has now been on crizotinib for 4 months with excellent tolerance, improved quality of life, and continued decrease in his tumor burden.

Patient and Tumor Characteristics
In an effort to further characterize cases of both ALK-positive and ALK-negative IMT, we obtained 37 samples from 33 patients with this rare disease (Table 1). Patients ranged in age from infancy (less than 1 year old) to age 41. As is typical for IMT, the tumors arose at multiple anatomic locations, including thorax, mesentry, peritoneum, and bladder. The pathologic diagnosis was established based on criteria according to the WHO classification (3). ALK IHC was completed on each sample as part of the standard pathologic evaluation (Supplementary Methods). Eleven of 37 (30%) of the cases were ALK IHC negative and 26 of 37 (70%) of the cases were ALK IHC positive.

Targeted NGS Identified ALK, ROS1, and PDGFRβ Tyrosine Kinase Fusions in a Collection of IMT Samples
We hypothesized that further insight into the biology of known fusions as well as discovery of novel kinase fusions would provide new therapeutic targets to treat patients with IMT. To address this hypothesis, we analyzed genomic DNA from all 37 IMT samples using a targeted NGS-based assay (FoundationOne), which assesses 3,769 exons of 287 cancer genes and 47 introns of 19 commonly rearranged genes,

Figure 1. Response to crizotinib in an 8-year-old boy with refractory IMT harboring a TFG–ROS1 fusion. A, schematic representation of the TFG–ROS1 fusion. ROS1 is located on chromosome 6q22 and TFG is located on 3q12. The breakpoint occurs in-frame between exon 4 of TFG and exon 36 of ROS1. B, CT scans before the initiation of crizotinib (left) and after 3 cycles of crizotinib (right) showing dramatic reduction in the tumor mass within the left lung. C, changes in Hgb, MCV, and ESR over the course of the patient’s treatments. Arrows below the graphs, initiation of the indicated therapies. The high (H) and low (L) limits of normal for each measured parameter are indicated on the blue graphs.
Multiple Actionable Kinase Fusions in IMT

**A**

**TFG** (chr3)

chr 3: 1,808,677

**ATG**

**TFG** exons 1–4

ROS1 exons 35–43

**TFG–ROS1 fusion**

**B**

**Pre-crizotinib**

**After 3 cycles of crizotinib**

**Hemoglobin (g/L)**

162.5
150.0
137.5
125.0
112.5
100.0
87.5
75.0

**MCV (fL)**

100
90
80
70
60
50

**ESR (mm/hr)**

125
100
75
50
25
0

**C**

**Hemoglobin (g/L)**

**MCV (fL)**

**ESR (mm/hr)**

Steroid pulse

Methotrexate + vinorelbine

Crizotinib (11/20/2013)
### Table 1. Summary of clinical characteristics and targeted NGS results for the study cohort

<table>
<thead>
<tr>
<th>Sample ID</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Tumor site</th>
<th>Tumor size (cm)</th>
<th>ALK IHC</th>
<th>Kinase fusion detected</th>
<th>Coverage</th>
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<td>F</td>
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<td>Pelvis</td>
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<td>Neg</td>
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<td>676</td>
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<td>L18</td>
<td>2</td>
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<td>8</td>
<td>Pos</td>
<td>TPM3–ALK</td>
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<tr>
<td>L22</td>
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<td>2</td>
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<td>Fail</td>
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<tr>
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<td>L24</td>
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<td>L25</td>
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<td>M</td>
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<td>8</td>
<td>Pos</td>
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<tr>
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<td>Pos</td>
<td>FN1–ALK*</td>
<td>511</td>
</tr>
<tr>
<td>L27</td>
<td>26</td>
<td>F</td>
<td>Bladder</td>
<td>7</td>
<td>Pos</td>
<td>CLTC–ALK</td>
<td>459</td>
</tr>
<tr>
<td>L28</td>
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<td>M</td>
<td>Mesentery</td>
<td>41</td>
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<tr>
<td>L29</td>
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<td>Pos</td>
<td>FN1–ALK*</td>
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<tr>
<td>L30</td>
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<td>Mesentery</td>
<td>8</td>
<td>Pos</td>
<td>Fail</td>
<td></td>
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<tr>
<td>L31</td>
<td>9</td>
<td>F</td>
<td>Lung</td>
<td>Unknown</td>
<td>Pos</td>
<td>CLTC–ALK</td>
<td>822</td>
</tr>
<tr>
<td>L32</td>
<td>4</td>
<td>F</td>
<td>Lung</td>
<td>Unknown</td>
<td>Pos</td>
<td>CLTC–ALK</td>
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<tr>
<td>L33</td>
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<td>Lung</td>
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<td>CLTC–ALK</td>
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<td>L34</td>
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<tr>
<td>L35</td>
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<td>PRKAR1A–ALK</td>
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<td>L36</td>
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<td>F</td>
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<tr>
<td>L37</td>
<td>6</td>
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<td>Lung</td>
<td>10.1</td>
<td>Neg</td>
<td>TFG–ROS1</td>
<td>660</td>
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</table>

**NOTE:** A total of 37 FFPE tumor samples from 33 different patients with IMT were included in the analysis. The following samples were obtained from the same patient at different times in his/her disease course: L3/L4, L7/L10, L31/L36, L32/L33/L34. There was 100% concordance in the kinase fusions detected across multiple samples from the same patient.

*Sufficient material was available to verify these kinase fusions with RNA sequencing.*

*Initial results from the FoundationOne genomic DNA analysis were negative. The FN1–ALK fusion, which harbors an atypical breakpoint within intron 18 of ALK, was detected by RNA sequencing.*
including 8 tyrosine kinases (Supplementary Table S2). This platform has been previously described and successfully used in several large genomic studies of various tumor types (10–12). In each case, tumor DNA was isolated from FFPE tissue. Average coverage was 543×. Targeted NGS was successfully performed in 22 of 26 ALK-positive and 11 of 11 ALK-negative specimens (Table 1 and Supplementary Fig. S2). In cases in which there was sufficient tumor material available, the kinase fusions were verified with RNA sequencing.

Among the 11 ALK IHC-negative cases, kinase fusions were identified in 8 of 11 (73%) of the cases (Table 1, Fig. 2A and B). Two cases harbored ALK fusions (sample L5, EML4–ALK; sample L9, TPM3–ALK), which were missed by ALK IHC testing alone. Among the other 9 ALK-negative samples, 4 contained distinct ROS1 fusions (sample L3/L4, YWHAE–ROS1; sample L6, TFG–ROS1), including the index patient (sample L37), and 2 contained a PDGFRβ fusion (samples L7/L10, NAB2–PDGFRβ). Notably, neither ROS1 nor PDGFRβ fusions have been described in IMT to date. The genomic coordinates for each fusion identified are summarized in Supplementary Table S3. Importantly, all kinase fusions identified in this study (ALK, ROS1, PDGFRβ) are therapeutically targetable with existing FDA-approved TKIs (8, 13–15).

Among the 11 ALK IHC-negative cases, kinase fusions were mutually exclusive. No other recurrent genomic alterations were identified by targeted NGS in these samples. B, schematic representation of the distinct ALK, PDGFRβ, and ROS1 fusions identified. In each case, the exons encompassed within each gene fusion partner are indicated.

DISCUSSION

IMT is a rare tumor that can arise at multiple anatomic locations. There are limited systemic therapeutic options available for patients with surgically unresectable and/or metastatic disease. Previous data have demonstrated that approximately 50% of IMTs are positive for ALK expression based on results from IHC. Responses to the TKI crizotinib have been documented in patients with ALK-positive IMT, demonstrating the importance of identifying this target (6, 14).

In our study, we successfully performed targeted NGS in 20 of 22 ALK IHC–positive IMT samples and identified several different ALK gene fusions, with various S′ gene fusion partners. Several of these fusion partners have been previously described, including TPM-3/4, ATIC, CLTC, CARS, and RANBP2 (5). However, we also identified novel ALK gene fusions, such as LMNA–ALK and PRKAR1A–ALK, the latter of which was detected in a congenital IMT. In addition,
we identified ALK fusions with noncanonical fusion breakpoints. FVII–ALK, which has previously been described in ovarian cancer, has a breakpoint in intron 18 of the ALK gene, whereas most fusions have a breakpoint in ALK intron 19 (16). Because patients with tumors harboring intron 1 (exon 19) ALK fusions can derive clinical benefit from ALK inhibitor therapy (17), there is a need to incorporate these atypical but recurrent fusions into NGS-based diagnostic platforms. Notably, we also detected ALK fusions in 2 of 11 IMT samples that tested negative for ALK expression by IHC. Therefore, the possibility of targeted therapy with an ALK inhibitor would have been missed for these patients with ALK testing by IHC alone.

In contrast, there are currently no data about potential oncogenic “drivers” in the ALK-negative subset of IMTs. We identified actionable kinase fusions in 8 of 11 ALK-negative IMT tumors analyzed by targeted NGS, including ROS1 and PDGFRβ kinase fusions, which have not yet been described in this disease. PDGFRβ kinase fusions have been described in myeloproliferative disorders (18). ROS1 kinase fusions have been detected in a variety of malignancies, including lung cancer, glioblastoma, cholangiocarcinoma, and Spitz tumors (reviewed in ref. 19). Crizotinib, which is FDA approved for the treatment of ALK fusion–positive lung cancer, is also a potent ROS1 inhibitor. Preliminary results from the phase I clinical trial of crizotinib in ROS1 fusion–positive lung cancer demonstrated an objective response rate of 36% (9). However, responses in other ROS1 fusion–positive cancers have not yet been documented. Here, we report that a young boy with ROS1 fusion–positive ALK tested negative by IHC. This was the first antitumor response this patient has experienced since his initial diagnosis more than 2 years before starting crizotinib; his tumor previously did not respond to four different lines of therapy, including cytotoxic chemotherapy or anti-inflammatory agents. His tumor mass decreased in size, his paraneoplastic anemia improved, and he felt better symptomatically. This case clearly illustrates the need for improved diagnostic and therapeutic paradigms in this disease.

Overall, our data show for the first time that kinase fusions are found in the majority of IMTs (85% in our series). To our knowledge, this study represents the largest genomic analysis of this tumor type to date, and our results redefine this heterogeneous disease as being largely a kinase fusion–driven neoplasm. These data not only provide insight into this rare disease but also offer rational targeted therapeutic strategies with existing FDA-approved TKIs based on the genomic profile of the tumor. Critical to successful deployment of this evolving therapeutic paradigm is incorporation of testing with highly sensitive NGS platforms capable of detecting both known and novel fusions in multiple oncogenes from a single tumor specimen.

METHODS

Patients and Tumor Samples

IMT samples and associated patient characteristics were analyzed with an Institutional Review Board–approved protocol (#090572). All clinical data were obtained and maintained according to Health Insurance Portability and Accountability Act (HIPAA) standards. All unique identifiers have been removed before publication.

Genomic DNA Sequencing and Analysis

DNA was extracted from FFPE samples. Sequencing was performed for 3,769 exons of 287 cancer genes and 47 introns of 19 commonly rearranged genes, including 8 tyrosine kinases (FoundationOne Panel; Supplementary Table S2) as previously described (10). Tumor content was assessed by hematoxylin and eosin staining before analysis; no micro/macro dissection tissue enrichment was performed. Sequencing was performed on the HiSeq2000 instrument (Illumina) with 40-bp paired reads to an average depth of 543X. Resultant sequences were analyzed for base substitutions, insertions, deletions, copy-number alterations, and select gene fusions (10). Additional information about the analytic validation of this assay as well as the sequencing of RNA is provided in the Supplementary Methods.

Disclosure of Potential Conflicts of Interest

C.M. Lovly reports receiving a commercial research grant from AstraZeneca, has received speakers’ bureau honoraria from Qiagen and Abbott Molecular, and is a consultant/advisory board member for Pfizer. D. Lipson is director of and has ownership interest (including patents) in Foundation Medicine. J.S. Ross is medical director of, reports receiving a commercial research grant from, and has ownership interest (including patents) in Foundation Medicine. P.J. Stephens has ownership interest (including patents) in Foundation Medicine, Inc. V.A. Miller is CMO of and has ownership interest (including patents) in Foundation Medicine. No potential conflicts of interest were disclosed by the other authors.

Authors’ Contributions

Conception and design: C.M. Lovly, D. Lipson, J.S. Ross, C.M. Coffin

Development of methodology: C.M. Lovly, D. Lipson, G. Otto, T. Brennan, J.S. Ross, V.A. Miller, C.M. Coffin

Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): C.M. Lovly, A. Gupta, C.T. Chung, S.C. Bornstein, J.S. Ross, C.M. Coffin

Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): C.M. Lovly, D. Lipson, J.S. Ross, P.J. Stephens, V.A. Miller, C.M. Coffin

Writing, review, and/or revision of the manuscript: C.M. Lovly, D. Lipson, C.T. Chung, S.C. Bornstein, J.S. Ross, P.J. Stephens, V.A. Miller, C.M. Coffin

Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): C.M. Lovly, T. Brennan, J.S. Ross, C.M. Coffin

Study supervision: C.M. Lovly, C.M. Coffin

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REFERENCES

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