# Intended Versus Inferred Treatment After <sup>18</sup>F-Fluoride PET Performed for Evaluation of Osseous Metastatic Disease in the National Oncologic PET Registry

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We have previously reported that PET with <sup>18</sup>F-fluoride (NaF PET) for assessment of osseous metastatic disease led to changes in intended management in a substantial fraction of patients with prostate or other types of cancer participating in the National Oncologic PET Registry. This study was performed to assess the concordance of intended patient management after NaF PET and inferred management based on analysis of Medicare claims. Methods: We analvzed linked post-NaF PET data of consenting National Oncologic PET Registry participants age 65 y or older from 2011 to 2014 and their corresponding Medicare claims. Post-NaF PET treatment plans, including combinations of 2 modes of therapy, were assessed for their concordance with clinical actions inferred from Medicare claims. NaF PET studies were stratified by indication (initial staging [IS] or suspected first osseous metastasis [FOM]) and cancer type (prostate, lung, or other cancers). Agreement was assessed between post-NaF PET intended management plans for treatment (surgery, radiotherapy, or systemic therapy) within 90 d for lung and 180 d for prostate or other cancers, and for watching (the absence of treatment claims for  $\geq 60$  d) as compared with claims-inferred care. Results: Actions after 9,898 scans were assessed. After NaF PET for IS, there was claims agreement for planned surgery in 76.0% (19/25) lung, 75.4% (98/130) other cancers, and 58.9% (298/506) prostate cancer. Claims confirmed chemotherapy plans after NaF PET done for IS or FOM in 81.0% and 73.5% for lung cancer (n = 148 and 136) and 69.4% and 67.5% for other cancers (n = 111 and 228). For radiotherapy plans, agreement ranged from 80.0% to 84.4% after IS and 68.4% to 74.0% for suspected FOM. Concordance was greatest for androgen deprivation therapy (ADT) (86.0%, n = 308) alone or combined with radiotherapy in prostate cancer IS (80.8%, n = 517). In prostate FOM, the concordance across all treatment plans was lower if the patients had ADT claims within 180 d before NaF PET. Agreement with nontreatment plans was high for FOM (87.2% in other cancers and 78.6% if no prior ADT in prostate) and low after IS (40.7%-

62.5%). **Conclusion:** Concordance of post–NaF PET plans and claims was substantial and higher overall for IS than for FOM.

Key Words: <sup>18</sup>F-fluoride PET; bone metastasis; prostate cancer; lung cancer; insurance claims linkage; outcomes and process assessment

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L he National Oncologic PET Registry (NOPR) was established as a response to the Centers for Medicare & Medicaid Services (CMS) Coverage with Evidence Development policy. We have previously reported results addressing the impact of PET on intended management of patients with cancer using prospectively collected data obtained before and after PET. NOPR initially assessed the impact of PET with <sup>18</sup>F-FDG (*1*,2), and a subsequent extension assessed the impact of <sup>18</sup>F-fluoride PET (NaF PET) for evaluation of osseous metastatic disease on cancer patient management (*3*–5).

The findings of the NOPR have been subject to 2 primary criticisms—first, that changes in planned management are only a surrogate for actual health outcomes, and second, that the dataset does not document the care actually delivered. Although this first criticism is valid, the underlying premise for using change in intended management as a surrogate for selection of appropriate care is based on the recognition that cancer care pathways in relation to disease stage (or extent) are, in general, well defined in practice guidelines. Hence, if an imaging test has been shown independently to have good performance for tumor detection and staging (as has been more than amply demonstrated for both <sup>18</sup>F-FDG PET and NaF PET), it can be reasonably surmised that selection of curative treatment for patients shown by the test to have low-stage disease will be appropriate, as will (vice versa) selection of palliative treatment for patients with distant metastatic disease.

In prior work, to address the second criticism for the <sup>18</sup>F-FDG PET dataset, we linked NOPR data with CMS claims from 2006 to 2008 and assessed the concordance between planned management

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and claims-inferred care for the 7 most common cancer types when the scans were obtained for initial staging of cancer or for restaging/detection of suspected recurrence (6,7). We found that there was moderate concordance between planned management and claims-inferred actions and that concordance was greater overall for initial staging than for uses of <sup>18</sup>F-FDG PET later in the cancer treatment continuum.

As part of the operational plan for the NaF PET registry, concurrent (quarterly) linkage to Medicare claims (for consenting participants with traditional fee-for-service Medicare) were to be provided to the NOPR investigators by CMS, and an analytic plan for assessment of these data was developed ( $\delta$ ). However, because of personnel resources and technical challenges, obtaining a near-concurrent claims dataset from CMS was not feasible, and this planned analysis did not occur in concert with other analyses of NOPR NaF PET data (3–5). As part of its 2015 National Coverage Decision Memorandum in response to a reconsideration request for coverage of NaF PET, CMS highlighted the failure to address the impact of NaF PET on more appropriate palliative (or curative) care, quality of life, or survival (9).

To address these concerns in part, Medicare claims available through the CMS Virtual Data Research Center (10) were requested for consenting NOPR participants for 2011–2014 (the most recent available) and were used to assess the concordance of intended and claims-inferred management of NOPR patients. The purpose of this analysis was to validate that actual management is generally concordant with planned management, thus further supporting the inference that change in intended management is a surrogate for selection of appropriate palliative or curative care.

#### MATERIALS AND METHODS

NOPR is a prospective data registry (ClinicalTrials.gov NCT00868582), the operational details and findings of which have been previously reported (1,2). The NaF PET component of the registry opened on January 31, 2011. Case report form revisions were implemented on January 27, 2012. The registry was closed to accrual on December 14. 2017.

For consenting participants who underwent NaF PET between February 6, 2011, and September 30, 2014, we linked NOPR data to their CMS claims by matching individual identifiers (social security number, sex, birth date) and the date of NaF PET. We assessed only the first PET requested for initial staging (IS) or for detection of suspected first osseous metastasis (FOM). We excluded patients younger than 65 y, those with Medicare Advantage (flagged in their Medicare records, for whom claims were thus not available), other scanning indications (diagnosis, unknown primary, suspected progression of osseous metastasis, and treatment monitoring), and those for whom no claim for NaF PET was paid.

## **Management Categories**

We limited our focus to post–NaF PET plans for treatment or watching and, therefore, excluded plans for additional imaging or biopsy. For each cancer type and indication, we assessed the most common single treatment (surgery, radiotherapy, chemotherapy, or androgen deprivation therapy [ADT]) or 2-category combination (e.g., radiotherapy and chemotherapy). Treatment plans for surgery or chemotherapy with a large diversity of second or third treatments were combined or collapsed into a "plus other" catch-all group: for example, surgery  $\pm$  other (secondary) treatments. For the 2 most common combination therapies (radiation + ADT and radiation + chemotherapy), we assessed complete (both) or partial (1 component) agreement. For each therapy type, we also counted the source of disagreement between the intended management plan and the claims-inferred management: other therapies or no therapy claims.

#### **Claims Definitions**

Appendix A lists the Current Procedural Terminology codes, the Health Care Common Procedure Coding System codes, and the National Drug Codes of approved therapies by cancer type. Surgery was defined by combining all thoracic and pelvic/prostate surgical codes as well as looking for surgical pathology and anesthesia Current Procedural Terminology codes. This avoided inappropriate inclusion of procedures for permanent venous access. Radiotherapy codes included all common techniques. ADT, focused specifically on use in prostate cancer, included a mix of parenteral (leuprolide, goserelin) and oral medications. Chemotherapy was interpreted broadly to include approved intravenous and oral agents, as well as infusional immunotherapy (excluding sipuleucel-T). Bone-targeted therapies, including infusional bisphosphonates or desunomab and radiopharmaceuticals, such as <sup>223</sup>Ra, were assessed but not reported herein.

The NOPR post–NaF PET forms did not collect information regarding the expected time frame of planned treatment. Given the usual greater urgency of action for lung cancer, we used a postscan claims window of 90 d for lung cancer and 180 d for prostate and other cancers. We therefore adjusted the last date of scan inclusion to June 30, 2014, for prostate and other cancers and September 30, 2014, for lung cancer.

#### Statistical Analysis

For each testing indication under each cancer type, the raw agreement was quantified by calculating the proportion of claimsinferred actual management to the post–NaF PET intended treatment plans. The 95% confidence interval was imputed using the Fisher exact test. All statistical analyses were performed using SAS version 9.4 (SAS Institute). We did not attempt to use any claims-based indices (such as the Klabunde index) to estimate comorbidity.

## RESULTS

#### **Defining Cohort and Clinical Characteristics**

Table 1 outlines the serial exclusions made in defining the analysis cohort of 9,898 patient scans—scan totals for lung, other, and prostate cancers, respectively, were 216, 496, and 2,701 for IS and

| TABLE 1      |        |  |  |  |  |  |  |
|--------------|--------|--|--|--|--|--|--|
| Defining the | Cohort |  |  |  |  |  |  |

| NOPR cases (2/6/2011 to 9/30/2014)   | n       |
|--|---------|
| Total number of cases  | 32,663  |
| Patient or provider: consent withheld  | (4,648) |
| Patient: no match to social security number  | (652)   |
| Patient: age $<$ 65 at time of scan  | (1,520) |
| Indication: cancer of unknown primary origin                                       | (266)   |
| Indication: diagnosis  | (1,078) |
| Indication: suspected progression of osseous<br>metastasis or treatment monitoring | (5,825) |
| Indication: subsequent scan performed for FOM                                      | (3,283) |
| Additional evaluation: post-NaF PET plan<br>to image or biopsy                     | (1,844) |
| Insurance: Medicare Advantage  | (2,184) |
| Insurance: no claims paid  | (566)   |
| No claim found for NaF PET   | (899)   |
| Analysis cohort  | 9,898   |
|  |         |

362, 1,374, and 4,749 for FOM (top of Table 2). The remainder of Table 2 provides selected characteristics of the cohort-median age and patient symptoms, signs, or other factors as indications for testing were similar to those in our prior reports. On the basis of the NaF PET assessment forms completed by interpreting physicians, the NaF PET scans in the cohort were read as negative (benign or equivocal) in 59.7%-81.4%, probable osseous metastasis in 5.8%-9.4%, and definite metastasis in 12.5%-31.0%; metastatic disease was multifocal in two-thirds of patients. The rates of hospitalizations, use of hospice within 60 d, and deaths within 180 d were all greatest in lung cancer and lowest in prostate cancer. Death within 180 d occurred in about one-third of patients with lung cancer, about 13% with other cancers, and in 1.7% with prostate cancer scanned for IS and 5.2% scanned for FOM.

## Concordance

Table 3 shows the agreement, including 95% confidence intervals, between various treatment categories stratified by treatment type, cancer type, and imaging indication. Planned surgeries were limited to patients undergoing IS and the numbers of patients with lung (n = 25) or other cancers (n = 130) were modest; there was 75.4%-76.0% claims concordance. In prostate cancer, plans for surgery (prostatectomy) were confirmed in only 58.9%, and 36.1% of these patients had claims for other treatments. This likely reflects the lack of consensus and importance of patient preferences in selection of treatment for newly diagnosed prostate cancer where radiation and ablative approaches are also used regularly.

Concordance with planned chemotherapy (either when used in combination with other actions or as the only planned treatment) in lung cancer patients was confirmed in 81.0% (n = 148) after IS scans and 73.5% (n = 136) after FOM scans and was modestly lower in other cancers: 69.4% for IS (n = 111) and 67.5% for FOM (n = 154). The absence of chemotherapy treatment claims, presumably because of either patient preference or incomplete Part D records (oral drug claims thus not available) were much more common after FOM scans (17.6% lung and 24.1% other

|   | Profile o  | f NOPR Coh | nort         |              |            |            |  |
|---|------------|------------|--------------|--------------|------------|------------|--|
|   | Lung       |            | Prostate     |              | Other      |            |  |
| Patient profile, indication, and findings   | IS         | FOM        | IS           | FOM          | IS         | FOM        |  |
| Number                                      | 216        | 362        | 2,701        | 4,749        | 496        | 1,374      |  |
| Age, median 25%–75% quartile (y)            | 73 (68–77) | 74 (69–80) | 73 (69–78)   | 76 (71–82)   | 75 (69–81) | 75 (70–80) |  |
| Symptoms, signs, or test results (%)        |            |            |              |              |            |            |  |
| None  | 70 (32.4)  | 43 (11.9)  | 1,574 (58.3) | 732 (15.4)   | 231 (46.6) | 142 (10.3) |  |
| Elevated or rising tumor marker or PSA only | *          | *          | 724 (26.8)   | 2,368 (49.9) | *          | 77 (5.6)   |  |
| Pain only                                   | 80 (37.0)  | 213 (58.8) | 142 (5.3)    | 683 (14.4)   | 165 (33.3) | 733 (53.3) |  |
| Evidence from other imaging                 | 28 (13.0)  | 40 (11.0)  | 117 (4.3)    | 293 (6.2)    | 49 (9.9)   | 145 (10.6) |  |
| Multiple                                    | 20 (9.3)   | 43 (11.9)  | 98 (3.6)     | 550 (11.6)   | 24 (4.8)   | 197 (14.3) |  |
| NaF PET findings (%)                        |            |            |              |              |            |            |  |
| Benign or equivocal                         | 139 (64.4) | 216 (59.7) | 2,198 (81.4) | 2,886 (60.8) | 391 (78.8) | 934 (68.0) |  |
| Probable metastases                         | 17 (7.9)   | 34 (9.4)   | 164 (6.1)    | 439 (9.2)    | 29 (5.8)   | 108 (7.9)  |  |
| Definite bone metastases                    |            |            |              |              |            |            |  |
| Unifocal                                    | 12 (5.6)   | 18 (5.0)   | 36 (1.3)     | 163 (3.4)    | 13 (2.6)   | 46 (3.3)   |  |
| Multifocal                                  | 41 (19.0)  | 80 (22.1)  | 227 (8.4)    | 951 (20.0)   | 47 (9.5)   | 206 (15.0) |  |
| Diffuse                                     | *          | 14 (3.9)   | 76 (2.8)     | 310 (6.5)    | 16 (3.2)   | 80 (5.8)   |  |
| Stage, post-NaF PET (%)                     |            |            |              |              |            |            |  |
| Local/NED                                   | 60 (27.8)  | 168 (46.4) | 1,974 (73.1) | 1,794 (37.8) | 288 (58.1) | 792 (57.6) |  |
| LN+/regional                                | 33 (15.3)  | 10 (2.8)   | 81 (3.0)     | 739 (15.6)   | 29 (5.8)   | 49 (3.6)   |  |
| Single metastases                           | 24 (11.1)  | 39 (10.8)  | 134 (5.0)    | 553 (11.6)   | 40 (8.1)   | 123 (9)    |  |
| Multiple metastases                         | 91 (42.1)  | 145 (40.1) | 393 (14.6)   | 1,663 (35.0) | 111 (22.4) | 410 (29.8) |  |
| Unknown                                     | *          | *          | 119 (4.4)    | *            | 28 (5.6)   | *          |  |
| Characteristics from claims                 |            |            |              |              |            |            |  |
| Hospitalized within 180 d after NaF PET (%) | 117 (54.2) | 157 (43.3) | 542 (20.0)   | 820 (17.2)   | 187 (37.7) | 349 (25.4) |  |
| Hospice within 60 d after NaF PET (%)       | 17 (7.9)   | 42 (11.6)  | *            | 60 (1.2)     | 13 (2.6)   | 54 (3.9)   |  |
| Death within 180 d after NaF PET (%)        | 68 (31.5)  | 128 (35.3) | 47 (1.7)     | 249 (5.2)    | 64 (12.9)  | 168 (12.2) |  |
| Medicare Part D claims found (%)            | 151 (69.9) | 223 (61.6) | 1,503 (55.6) | 2,668 (56,1) | 303 (61.0) | 848 (61.7) |  |

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\*Cell count < 11.

PSA = prostate-specific antigen; NED= no evidence of disease; LN+ = lymph nodal disease positive.

Data in parentheses are percentages.

 TABLE 3

 Concordance of NOPR Post-PET Treatment Plans and Claims-Inferred Care

| NOPR treatment plan  | Cancer<br>type | Imaging indication | No. of patients | Agreement (%) | 95 confidence<br>interval of agreement (%) | Other<br>treatments | No treatment claims |
|----------------------|----------------|--------------------|-----------------|---------------|--|---------------------|---------------------|
| Surgery              | Lung           | IS                 | 25              | 19 (76.0)     | 54.9–90.6                                  | *                   | *                   |
|                      | Other          | IS                 | 130             | 98 (75.4)     | 67.1–82.5                                  | 21 (16.1)           | 11 (8.5)            |
|                      | Prostate       | IS                 | 506             | 298 (58.9)    | 54.5-63.2                                  | 183 (36.1)          | 27 (5.3)            |
| Chemotherapy ± other | Lung           | IS                 | 148             | 120 (81.0)    | 73.8–87.1                                  | 20 (13.5)           | *                   |
|                      | Lung           | FOM                | 136             | 100 (73.5)    | 65.3-80.7                                  | 12 (8.8)            | 24 (17.6)           |
| Chemotherapy only    | Other          | IS                 | 111             | 77 (69.4)     | 59.9–77.8                                  | 16 (14.4)           | 18 (16.2)           |
|                      |                | FOM                | 228             | 154 (67.5)    | 61.0–73.6                                  | 19 (8.3)            | 55 (24.1)           |
| Radiation            | Lung           | IS <sup>‡</sup>    | 80              | 67 (83.7)     | 73.8–91.1                                  | *                   | *                   |
|                      |                | FOM <sup>‡</sup>   | 36              | 26 (72.2)     | 54.8-85.8                                  | *                   | *                   |
|                      | Other          | IS <sup>†</sup>    | 30              | 24 (80.0)     | 61.4–92.3                                  | *                   | *                   |
|                      |                | FOM <sup>†</sup>   | 54              | 40 (74.0)     | 60.3-85.0                                  | *                   | *                   |
|                      |                | FOM <sup>‡</sup>   | 59              | 36 (61.0)     | 47.4–73.4                                  | *                   | *                   |
|                      | Prostate       | IS <sup>†</sup>    | 729             | 616 (84.4)    | 81.7-87.1                                  | 75 (10.3)           | 38 (5.2)            |
|                      |                | FOM <sup>†</sup>   | 422             | 289 (68.4)    | 63.8–72.9                                  | 60 (14.2)           | 73 (17.3)           |
| ADT only             | Prostate       | IS                 | 308             | 265 (86.0)    | 81.7-89.7                                  | 27 (8.8)            | 16 (5.2)            |
|                      |                | FOM                | 1,088           | 895 (82.3)    | 79.9–84.5                                  | 36 (3.3)            | 157 (14.4)          |
| ADT + radiation      | Prostate       |                    |                 |               |  |                     |                     |
| ADT component        |                | IS                 | 517             | 418 (80.8)    | 77.2-84.1                                  | 17 (3.3)            | 15 (2.9)            |
|                      |                | FOM                | 271             | 205 (75.6)    | 70.1-80.6                                  | *                   | 29 (10.7)           |
| Radiation component  |                | IS                 | 517             | 424 (82.0)    | 78.4-85.2                                  | 17 (3.3)            | 15 (2.9)            |
|                      |                | FOM                | 271             | 183 (67.5)    | 61.6–73.1                                  | *                   | 29 (10.7)           |
|                      |                |                    |                 |               |  |                     |                     |

\*Cell count < 11.

<sup>†</sup>Radiation component of plans of radiation plus chemotherapy.

<sup>‡</sup>Radiation therapy only.

Data in parentheses are percentages.

cancers) than claims for other treatments (8.3% and 8.8%). In prostate cancer, chemotherapy agreement was low, especially in men with no prior ADT claims (Table 3), with just under one-half of men having other treatment claims. Restricting the prostate cancer analysis to men with Part D claims did not improve the rate of agreement, indicating that almost all the prostate cancer chemotherapies were intravenous infusion therapies.

Radiotherapy plans were infrequent, with total counts of under 100 patients in lung and other cancers for each indication. Concordance rates were slightly higher after IS (80+%) than FOM scans (61%-74%). Claims concordance for radiotherapy after IS scans for prostate cancer was much higher (84.4% alone or 82.0% with ADT) than concordance for surgery (n = 506, 58.9%). Concordance with radiotherapy minimally differed when it was planned as the sole treatment or if it was used in combination with ADT in both indications.

ADT either as the only treatment or as part of a planned combination with radiotherapy after IS for prostate cancer had the highest agreement (80.8%–86.0%), and only 2.9%–5.2% of these patients had no treatment claims.

Table 4 shows that the rates of agreement with post–NaF PET plans for therapies were all higher in prostate cancer patients who had had claims-inferred ADT in the preceding 6 mo than in those who did not (Table 4). For example, patients with post–NaF PET

plans of ADT only (reflecting a continuation of therapy) had a 90.5% agreement versus 76.9% with no prior ADT. The rate of agreement with planned chemotherapy was much higher in patients with (51.2%) than in those without prior ADT (30.7%), and the converse was true with the frequencies of no treatment claims, being much more frequent if no prior ADT versus if ADT claims (20.8% vs. 5.4%).

Table 5 shows the agreement when the plan submitted to NOPR was for nontreatment (e.g., watch, supportive care, hospice) and no treatment was demonstrated by claims in the 60 d after NaF PET. Patients with prostate (40.7%) and other cancer (45.1%) had some type of treatment claims within 60 d of IS scanning. The absence of treatment claims was much greater after FOM scans—75.6%–87.2% of lung, other cancer, or prostate cancer patients with prior ADT claims did not have treatment claims. Almost half of prostate cancer patients with prior ADT claims in whom the plan was watching continued to have post–NaF PET ADT claims, suggesting that providers may not have viewed ADT continuation as a treatment plan.

## DISCUSSION

Assessments of how often physicians' intended management of cancer patients (e.g., based on data from a survey, registry, or

 
 TABLE 4

 Agreement in Post–NaF PET Plans for Scans Obtained for Suspected FOM of Prostate Cancer Stratified by Prior ADT Claims

| NOPR treatment plan  | Prior ADT | No. of patients | Agreement (%) | 95 confidence<br>interval of agreement (%) | Other<br>treatments | No treatment claims |
|----------------------|-----------|-----------------|---------------|--|---------------------|---------------------|
| ADT only             | Yes       | 430             | 389 (90.5)    | 87.3–93.1                                  | 11 (2.6)            | 30 (6.9)            |
|                      | No        | 658             | 506 (76.9)    | 73.5–80.1                                  | 26 (3.9)            | 126 (19.3)          |
| Radiation only       | Yes       | 117             | 86 (73.5)     | 64.6-81.2                                  | 28 (23.9)           | *                   |
|                      | No        | 305             | 203 (66.6)    | 61.0–71.8                                  | 34 (11.1)           | 68 (22.3)           |
| ADT + radiation      |           |                 |               |  |                     |                     |
| ADT component        | Yes       | 83              | 74 (89.2)     | 80.4–94.9                                  | *                   | *                   |
|                      | No        | 188             | 131 (69.7)    | 62.6–76.2                                  | *                   | *                   |
| Radiation component  | Yes       | 83              | 63 (75.9)     | 65.3-84.6                                  | *                   | *                   |
|                      | No        | 187             | 120 (63.8)    | 56.5-70.7                                  | *                   | *                   |
| Chemotherapy ± other | Yes       | 406             | 208 (51.2)    | 46.3–56.2                                  | 176 (43.3)          | 22 (5.4)            |
|                      | No        | 264             | 81 (30.7)     | 25.2–36.6                                  | 128 (48.5)          | 55 (20.8)           |
|                      |           |                 |               |  |                     |                     |

\*Cell count < 11.

interview at a multidisciplinary clinic before the patient encounter) is actually delivered have rarely been reported (11). The reliability of intended management as a surrogate endpoint is dependent on the quality and depth of evidence or consensus reported in clinical practice guidelines or algorithms. For example, there is a high level of consensus that surgical excision for patients with no evidence of metastases after imaging for IS of lung or many other cancers is appropriate, but much lower consensus would be expected for an intended management plan of chemotherapy for men scanned for FOM of prostate cancer (as well as many women with breast cancer) who have not yet received hormonal therapy.

The assessment of change in intended management has been an integral part of the NOPR and evaluations of <sup>18</sup>F-FDG PET in similar analyses in Australia and Canada (12-14). We previously reported that the concordance between NOPR postscan intended

#### TABLE 5

NOPR Plans for Nontreatment (Watch, Supportive Care, Hospice) and Absence of Treatment Claims Within 60 Days

| Cancer<br>type                       | Imaging indication   | No. of patients | Agreement<br>(%) | 95 confidence<br>interval of<br>agreement (%) |  |  |
|--------------------------------------|----------------------|-----------------|------------------|---|--|--|
| Lung                                 | IS                   | 24              | 15 (62.5)        | 40.6–81.2                                     |  |  |
| Other                                | IS                   | 113             | 51 (45.1)        | 35.8–54.8                                     |  |  |
| Prostate                             | IS                   | 391             | 159 (40.7)       | 35.8–45.7                                     |  |  |
| Lung                                 | FOM                  | 180             | 136 (75.6)       | 68.1–81.6                                     |  |  |
| Other                                | FOM                  | 798             | 696 (87.2)       | 84.7–89.5                                     |  |  |
| Prostate                             | FOM, prior<br>ADT    | 461             | 203 (44.1)       | 39.4–48.7                                     |  |  |
|                                      | FOM, no<br>prior ADT | 1,340           | 1,053 (78.6)     | 76.3–80.7                                     |  |  |
| Data in parentheses are percentages. |                      |                 |                  |   |  |  |

management and claims-inferred actual management is much higher after <sup>18</sup>F-FDG PET done for IS to help plan an initial treatment strategy than when PET is used to evaluate suspected cancer recurrences (6,7). Overall, for NaF PET, the level of agreement between pre-PET intended management and claims-inferred actual management is similar to that we have previously reported for <sup>18</sup>F-FDG PET.

In our prior NaF PET reports, we noted that referring physicians indicated that other advanced imaging would have been planned in 50%–70% of cases, if NaF PET were not available. After NaF PET, the relative frequencies of definite osseous metastatic disease were similar with IS or FOM by cancer types, and the frequency of treatment as intended management was much higher in prostate cancer than in lung or other cancer types (3,4). These differences likely reflect differences in management of nonosseous disease as well as NOPR's limitation of not having documentation of the current or preceding systemic therapies. This is one of the reasons we limited this analysis to patients scanned for IS and FOM and excluded those scanned for suspected progression of known osseous metastasis or treatment monitoring, since ongoing or prior treatments were not known as well as our prior difficulties in assessing treatment monitoring after <sup>18</sup>F-FDG PET (5).

In our analysis of the concordance between NOPR intended and claims-inferred actual management of patients after NaF PET, we recognize that the assessment of claims-inferred chemotherapy has the well-documented problem of incomplete claims for identifying oral chemotherapies (15). Our analysis is similar to others in that just over half of patients had Medicare Part D claims. Disagreement was higher for chemotherapy plans for FOM than for IS, likely reflecting a combination of greater use of oral chemotherapies and the more limited benefits of chemotherapy late in the trajectory of disease. This leads patients to decline chemotherapy. Additionally, a rapidly deteriorating performance status may lead physicians to change the plan to supportive care or hospice.

There are no known benchmarks for addressing the appropriate role for "surrogate" endpoints in oncology (16). For this analysis,

there is no known minimal threshold of agreement between registrybased intended management and inferred management based on claims. Despite this, we believe our current results, which generally show a high degree of concordance where there is greater consensus of treatment effectiveness and/or low toxicity, when combined with our prior reports of the impact of NaF PET on change in management (6,7), broadly demonstrate that management plans based on NaF PET are associated with actual and appropriate care. On the basis of these findings in combination with the results from two independent metaanalyses (17,18) showing superior diagnostic performance of NaF PET compared with conventional bone scintigraphy for detection of osseous metastasis, the use of NaF PET as a tool to guide management of patients with cancer is a rational strategy for selecting appropriate curative or palliative care.

## CONCLUSION

Concordance of post–NaF PET plans and actual care inferred from Medicare claims is substantial, is greater overall for IS than for FOM, and supports the use of NaF PET as a beneficial tool to guide the management of patients with cancer.

#### DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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## APPENDIX A: COMMON PROCEDURAL AND DRUG CODES USED IN ANALYSIS

Chemotherapy Procedure Codes

90765-90779, 96401-96549

- Chemotherapy Drugs for infusion therapies and selected oral drugs
- J9264, J9305, J9035, j9045, J9060, J9065, J9308, J9170, J9171, J9201, J9230, J9260, J8610, J9264, J9265, J9293, J9043, C9027, J9308, C9025, J9360, J9390, J8999, C9399, abiraterone, enzalutamide

Prostate Cancer Hormonal Therapies

J9155, J9217, J9218, J9219, J9202, J9255, flutamide, bicalutamide, nilutamide

Surgical Pathology and Cytology Codes

88104-88112, 88142, 88160-88175, 88300-88309, 88321, 88331-88334

Anesthesia (surgery)

00100-01860, 01996 (excluding subcutaneous intravenous lines, such as Port-a-cath)

#### Radiotherapy

77014, 77261-77263, 77280-77299, 77300-77373, 77401-77421, 77427-77499, 77520-77525, 77750-77799

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