Prevalence of clinically significant incidental findings by whole-body fludeoxyglucose F 18 positron emission tomography/computed tomography scanning in moderate-to-severe psoriasis patients participating in clinical trials

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Background: There has been an increase in the number of psoriasis treatments being investigated in clinical trials. Patients may have undiagnosed issues at the start of a study which may become identified during follow-up as incident medicinal conditions. The prevalence of incidental findings in patients with moderate-to-severe psoriasis presenting for clinical trials is unknown.

Objective: Determine the prevalence of incidentalomas and rate of malignancy identified by fludeoxyglucose F 18 (FDG) positron emission tomography/computed tomography (PET/CT) imaging in clinical trial patients with moderate-to-severe psoriasis.

Methods: A cross-sectional secondary analysis of patients with moderate-to-severe psoriasis who underwent FDG PET/CT scans at the baseline visit, before randomization, for 3 phase 4 clinical trials on vascular inflammation in psoriasis. Only patients without active infection, malignancy, or uncontrolled comorbidities were eligible for the clinical trials.

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Results: A total of 259 healthy patients with moderate-to-severe psoriasis underwent an FDG PET/CT scan as part of the study procedures. In all, 31 patients (11.97%) (95% confidence interval [CI], 8.28-16.56) had clinically significant incidentalomas on the baseline FDG PET/CT scan. Univariate logistic regression demonstrated that with every increase of 10 years of age, there was an approximate 30% increased risk of discovery of an incidentaloma (odds ratio, 1.30; 95% CI, 1.01-1.68). Of those patients with findings suggestive of malignancy (n = 28), 6 were confirmed to have cancer, resulting in a 2.31% (95% CI, 0.9-5.0) prevalence of malignancy. The positive predictive value of a true cancer was 31.58% (range, 21%-54%).

Limitations: Generalizability and lost to follow-up.

Conclusion: Incidentalomas on FDG PET/CT imaging are common in otherwise healthy, asymptomatic patients with moderate-to-severe psoriasis in clinical trials. Our results can help inform interpretation of clinical trial safety data and emphasize the importance of compliance with cancer screening recommendations. (J Am Acad Dermatol 2019;80:1630-9.)

Key words: biologics; FDG PET/CT; incidental findings; psoriasis; randomized controlled trials.

CAPSULE SUMMARY

- The prevalence of serious medical problems not detected by routine history, physical examination, or laboratory studies in patients with moderate-to-severe psoriasis presenting for clinical trials is not known.
- About 12% of patients had clinically significant incidental findings on fludeoxyglucose F 18 positron emission tomography/computed tomography imaging, and 2.31% of patients had cancer.

Psoriasis is a chronic, systemic, inflammatory disease that affects approximately 125 million people worldwide. About 20% of patients with psoriasis have moderate-to-severe skin disease and may be candidates for treatment with phototherapy or oral or injectable (eg, biologic) medications.[1] Patients with psoriasis, particularly when the disease is severe, have an increased incidence and prevalence of major comorbidities, including cardiovascular disease, metabolic disease, and malignancy.[2-5] There has been a revolution in the treatment of moderate-to-severe psoriasis over the past 2 decades, with multiple novel agents being investigated in clinical trials. In clinical research, some medical conditions may not be diagnosed at the start of the study but seemingly appear during the course of the study or follow-up, which can affect assessments of drug safety. Therefore, it is of special interest to understand which types of major medical problems may be undiagnosed at the start of a clinical trial and identified during follow-up as incident medical conditions.

We have been conducting a series of clinical trials to determine the impact of several different psoriasis treatments on markers of cardiovascular disease by using fludeoxyglucose F 18 (FDG) uptake detected and measured on positron emission tomography/computed tomography (PET/CT). This technique was used as a primary end point, as it allows for measurement of aortic vascular inflammation that is reliable, predictive of cardiovascular events, and rapidly responsive (eg, within 4-12 weeks) to treatments known to lower cardiovascular risk, such as statins.[6] FDG PET/CT imaging is also highly sensitive, but not necessarily specific, for conditions characterized by increased metabolic activity, such as cancer.[7] As a result, the use of FDG PET/CT for research purposes may give rise to incidentalomas, which are findings that are unexpected in an asymptomatic patient or findings in a symptomatic patient that are unrelated to the reason for which the investigation was ordered.[8-10] Incidentalomas are estimated to affect tens of thousands of human subjects involved in imaging research annually in the United States,[8] but little research has reported the rates and types of incidentalomas found in clinical trials of patients with a chronic inflammatory disease such as psoriasis. Therefore, the aim of this study was to evaluate the prevalence of previously unfound clinically significant medical problems identified by baseline FDG PET/CT imaging in clinical trial patients with moderate-to-severe psoriasis.

METHODS

Study design and patient selection

This was a cross-sectional secondary analysis of patients with moderate-to-severe psoriasis who were screened and underwent baseline FDG PET/CT scans for 3 phase 4 clinical trials: Vascular

Abbreviations used:

CI: confidence interval
CT: computed tomography
FDG: fludeoxyglucose F 18
PASI: Psoriasis Area and Severity Index
PET: positron emission tomography
SD: standard deviation
VIP: Vascular Inflammation in Psoriasis

Inflammation in Psoriasis (VIP), which was conducted at 9 sites; VIP-Secukinumab, which was conducted at 12 sites, and VIP-Ustekinumab, which was conducted at 1 site. Adult patients with moderate-to-severe plaque psoriasis, defined by at least 10% body surface area involvement and a Psoriasis Area and Severity Index (PASI) score of 12 or higher, were screened for eligibility. Only healthy patients were eligible for the 3 clinical trials. Patients with medically significant, uncontrolled comorbidities (eg, unstable ischemic heart disease, congestive heart failure, uncontrolled hypertension, recent cerebrovascular accidents, diabetes mellitus, psychiatric disease requiring frequent hospitalization) were excluded for the primary purpose of the clinical trial. Furthermore, patients with a history of demyelinating disease, systemic lupus erythematosus, or hematologic or solid malignancy within the past 5 years (except for successfully treated basal cell carcinoma, nonmetastatic cutaneous squamous cell carcinoma, or cervical carcinoma in situ) were also excluded. To determine eligibility for the trial, recruited patients attended a screening visit during which baseline demographics and a thorough clinical history were obtained and a full physical examination and laboratory testing (blood count; tests of kidney and liver function; and screening for HIV, hepatitis B and C, and tuberculosis infections) were performed. Specifically, the required laboratory values were as follows: hemoglobin level higher than10 g/dL in females or higher than12 g/dL in males, white blood cell count between 2.5 and 15 $\times$ 10^9/L (if the white blood cell count was <2.5 $\times$ 10^9/L, the subject could be included as long as absolute neutrophil count was >1000 cells/mm^3), platelet count higher than 100 $\times$ 10^9/L, creatinine level less than 1.6 mg/dL (<141 μmol/L), aspartate transaminase or alanine transaminase level less than 2.5 upper limits of normal, and total bilirubin level no more than 2 mg/dL ($\leq$26 μmol/L). Further details of the primary outcomes and methodology have been published previously[11] and reported on ClinicalTrials.gov (NCT01553058, NCT02690701, and NCT02187172).[12-14] Study approval for the clinical trials was obtained from the institutional review board at the University of Pennsylvania or the respective local institutional review board when indicated. All study participants provided written informed consent. This article was prepared according to the Strengthening the Reporting of Observational Studies in Epidemiology statement.[15]

Outcomes and classification

Incidental findings, which served as the outcome of interest, were defined as observations of potential clinical significance that were discovered and either unrelated to the purpose or beyond the aims of the research studies in healthy, asymptomatic subjects or symptomatic patients with seemingly nonsuggestive symptoms. This definition of incidentaloma is similar to definitions described in previous research studies[8,10] and clinical practice.[9] In our study, an incidentaloma was considered clinically significant when the board-certified radiologist recommended further work-up with additional laboratory testing, imaging, or invasive procedures (eg, biopsy). If a patient had more than 1 incidentaloma, the classification was based on the incidentaloma belonging to the most severe category because that would dictate whether the patient required further work-up. As a sensitivity analysis, a separate classification method proposed by Lumbreras et al was also utilized. Each clinically significant incidental finding was categorized as major (may cause mortality), moderate (may cause morbidity), minor (hardly relevant and likely to require no follow-up), or unclassified (not categorized in the aforementioned classification system).[16]

Data collection

All patients who met the screening criteria underwent a whole-body (ie, skull vertex to toes) FDG PET/CT scan approximately 60 to 120 minutes (range of delay, 48-146 minutes) following intravenous administration of approximately 15 mCi of FDG (or weight-based dosing for the VIP-Secukinumab study) during the baseline visit at the respective medical centers in the United States. Radiologic images were interpreted by a board-certified radiologist experienced in the interpretation of FDG PET/CT scan imaging. Patients without clinically significant incidental findings on FDG PET/CT were randomized and started the intervention phase of the respective study. We reviewed the reports for all patients with clinically significant incidental findings. As part of the study procedures, these patients underwent additional evaluation and were randomized if the clinically significant

Table I. Baseline characteristics of patients with psoriasis (N = 259)

Characteristic	Value
Sex, n (%)	
Female	82 (31.66%)
Male	177 (68.34%)
Mean age, y (SD)	45.31 (14.70)
Age range, y	19-83
Race, n (%)	
American Indian/Native American	1 (0.39%)
Asian	18 (6.95%)
African American	21 (8.11%)
White	202 (77.99%)
Other	17 (6.56%)
Ethnicity, n (%)	
Hispanic/Latino	54 (20.85%)
Non-Hispanic/Non-Latino	202 (77.99%)
Missing	3 (1.16%)
BMI, kg/m^2	
Mean (SD)	31.83 (7.47)
Range	18.00-58.72
Missing, n (%)	3 (1.16%)
Smoking status, n (%)	
Never	126 (48.65%)
Current	57 (22.01%)
Former	73 (28.19%)
Missing	3 (1.16%)
Median alcohol units consumed/wk (IQR)	1 (1-7)
History of biologic treatment, n (%)	84 (32.43%)
History of phototherapy, n (%)	74 (28.57%)
History of oral systemic treatment, n (%)	71 (27.41%)
Mean body surface area (SD)	24.80 (16.33)
Mean Psoriasis Area and Severity Index score (SD)	19.22 (9.15)

BMI, Body mass index; *IQR*, interquartile range; *SD*, standard deviation.

incidental finding was not deemed to be relevant to the safety of the treatments being studied. Subsequent recommendation for work-up was categorized as clinical correlation, additional laboratory testing, imaging, or invasive procedures (eg, biopsy). Available research visit notes and pathology reports were reviewed to confirm neoplastic status.

Data analysis

The exposure was FDG PET/CT baseline imaging. Some patients underwent baseline imaging for multiple VIP studies, so we included only findings from each patient's first baseline scan for our analyses. The outcomes of interest were (1) the prevalence of clinically significant incidentalomas and (2) the rate of malignancy. Of the patients who underwent baseline imaging, we evaluated the number with a confirmed cancer diagnosis to find the rate of malignancy.

From the extracted data, we summarized ranges for continuous data and calculated proportions and percentages for categoric data with 95% confidence interval (CI). Logistic regression was performed to identify baseline characteristics that might predict a clinically significant incidental finding. Data management and statistical analyses were performed with STATA software (version 15.1, StataCorp, College Station, TX).

RESULTS

A total of 259 patients who had moderate-to-severe psoriasis with no evidence of active or poorly controlled medical conditions and had undergone a physical examination and laboratory evaluation without clinically significant findings underwent an initial FDG PET/CT scan at the baseline visit as part of the screening phase for the 3 clinical trials. Baseline characteristics of the study population are summarized in Table I. The majority of the patients were white males, with an average body mass index of 31.83 (standard deviation [SD], 7.47) and a mean age of approximately 45 years (SD, 14.70).

Of the 259 patients, 31 (11.97% [95% CI, 8.28-16.56]) had clinically significant incidental findings on the baseline FDG PET/CT scan; their mean age was 50.61 years (SD 14.71). In all, 15 patients (5.79% [95% CI, 3.27-9.37]) had major findings, 10 patients (3.86% [95% CI, 1.87-6.99]) had moderate incidentalomas, and 4 patients (1.54% [95% CI, 0.4%-3.9%]) had minor incidentalomas according to the classification system developed by Lumbreras et al. An additional 2 patients

$$\text{Prevalence} = \frac{\text{Patients with} \geq 1 \text{ incidentaloma}}{\text{Total patients who underwent baseline imaging}}$$

$$\text{Malignancy rate} = \frac{\text{Patients with} \geq 1 \text{ malignancy}}{\text{Total patients who underwent baseline imaging}}$$

Table II. Rates of clinically significant incidental findings in the VIP trials

Total baseline scans	Patients with clinically significant incidental findings, n %	*British Journal of Radiology* classification*							
		Major		Moderate		Minor		Unclassified (benign)	
259	31 (11.97%)	15	5.79%	10	3.86%	4	1.54%	2	0.77%
		Malignancy status							
		Confirmed malignancy		Unknown		Benign			
		6	2.32%	9	3.47%	16	6.18%		

Clinically significant as defined by requiring work-up from the radiologist or dermatologist.
*Major findings (may cause mortality), moderate findings (may cause morbidity), minor findings (hardly relevant and no follow-up needed), and unclassified (benign findings not mentioned in the classification system). If a patient had more than 1 incidentaloma, the classification was based on the incidentaloma belonging to the most severe category, as that would dictate whether the patient required further work-up.

(0.77% [95% CI, 0.09%-2.76%]) had benign incidentalomas that could not be categorized according to the aforementioned system (Table II).[16] The major and moderate categories corresponded to our study definition of clinically significant incidentalomas, as diagnoses in those categories were likely to require further work-up. Univariate logistic regression demonstrated that with every increase of 10 years of age (decile), there was an approximately 30% increased risk of discovery of a clinically significant incidentaloma as determined by both classification methods (odds ratio, 1.30 [95% CI, 1.01-1.68]). No association was seen with sex, smoking, alcohol use, history of oral systemic or biologic treatment use, body mass index, or psoriasis severity as measured by PASI score.

The clinical suspicion and course of disease in the patients with clinically significant incidental findings are described in Table III. Of the 31 incidentalomas found in patients, 7 (22.58% [95% CI, 9.59-41.10]) were found in the lungs, 6 (19.35% [95% CI, 7.45-37.47]) were found in the head and neck region, 5 (16.13% [95% CI, 5.45-33.73]) were found in the colon, and 3 (9.68% [95% CI, 2.04-25.75]) were found in the pelvis. There was 1 incidentaloma (3.2% [95% CI, 0.08-16.70]) found in each of the following locations: adrenal gland, bone, esophagus, inguinal area, kidney, liver, mediastinum, prostate gland, rectum, and stomach. In the 31 patients with clinically significant incidentalomas, further investigation was needed for 1 patient owing to suspicion of an arachnoid cyst and 2 patients had findings suggestive of infection. Overwhelmingly, most findings were suggestive of malignancy (n = 28). Cancer was confirmed in 6 patients (gastrointestinal stromal tumor of the small bowel, oropharyngeal adenocarcinoma, uterine leiomyosarcoma, lymphoma, papillary thyroid carcinoma, and non–small cell lung adenocarcinoma), yielding an overall prevalence of malignancy in the study population of 2.31% (95% CI, 0.9-5.0). The 6 patients with confirmed cancer had a mean age of 66.5 years (SD, 9.29). In all, 9 patients with findings concerning for cancer were lost to follow-up. The positive predictive value of a clinically significant neoplastic incidental finding for being a true cancer was 31.58%. The positive predictive value ranged from 21% (assuming that all 9 patients for whom follow-up information was unobtainable did not have cancer) to 54% (if all patients lost to follow-up did, in fact, have cancer).

DISCUSSION

To our knowledge, this is the first large multicenter study to report the frequency and outcomes of incidental findings with the use of noninvasive imaging in patients with psoriasis. The results of our study demonstrate that there is an approximately 12% prevalence of clinically significant imaging findings in a population of patients with moderate-to-severe psoriasis who are asymptomatic and have an unremarkable history, physical examination, and laboratory work-up. In total, 6 patients (2.3%) had a serious underlying cancer that necessitated further follow-up or work-up. The true rate of cancer in this population may be as high as 6% (n = 15) if all suspected neoplasms for which we were unable to obtain follow-up information are true malignancies. These findings have important implications for clinical trials and clinical practice. For example, we identified 1 case of lung adenocarcinoma in a patient with a history of smoking that, in daily clinical practice, could have potentially been identified by routine screening in accordance with US Preventive Services Task Force recommendations, emphasizing the importance of encouraging patients to be up-to-date with age-appropriate cancer screening recommendations.[17] Although the lung adenocarcinoma may have been detected by recommended screening, it is possible that the other cancers (gastrointestinal stromal tumor of the small bowel,

Table III. Clinical course of patients with clinically significant incidental findings

Age, y	Sex	Race	Clinical suspicion/ differential diagnosis	Related medical history	Recommendation	Additional work-up undertaken	Diagnosis (last known clinical course)	Randomized*	Study course†
Malignancy diagnosed									
55	F	White	Underlying malignancy (eg, SCC of soft palate, cancer of minor salivary gland, infectious or inflammatory etiologies)	No history of cancer	Biopsy	Endoscopic correlation	Polymorphous low-grade adenocarcinoma (T1N0M0)	No	Discontinued
57	F	White	Postmenopausal endometrial thickening from degenerated leiomyoma or uterine malignancy	PCP previously investigated; biopsy showed noncycling endometrium	Pelvic MRI	Hysterectomy for ongoing symptoms	Pathology of the uterus revealed leiomyosarcoma contained within the uterus	Yes	Discontinued
65	M	White	Adrenal metastasis, small bowel (lymphoma, GIST, carcinoid tumor)	N/A	Abdominal MRI	MRI; f/u with specialist	GIST of the small bowel stage T2N0M0G1, IA, KIT exon 11 (excision and radiation of neoplasms)	No	Discontinued
69	M	White	Bilateral inguinal and obturator chain lymphoma	N/A	Biopsy	Biopsy	Bilateral inguinal and obturator chain lymphoma	No	Discontinued
76	M	White	Thyroid nodule	Basal cell carcinoma, SCC, prostate cancer	Biopsy	Biopsy	Papillary thyroid carcinoma (unknown stage)	No	Discontinued
77	M	African American	Lung carcinoma (vasculitis, lymphoma, and cryptogenic organizing pneumonia)	Denies any toxic, asbestos or TB exposures; smoke 1 cigarette pack/d for 50 y	Clinical correlation and scan	Bronchoscopy, then chemotherapy	Non−small cell lung adenocarcinoma (stage IV T2bN0M1a with pleural metastases, EGFR/ALK wild-type)	No	Discontinued

Continued

Table III. Cont'd

Age, y	Sex	Race	Clinical suspicion/ differential diagnosis	Related medical history	Recommendation	Additional work-up undertaken	Diagnosis (last known clinical course)	Randomized*	Study course†
Malignancy not diagnosed (benign or unknown findings)									
21	M	White	Pulmonary nodule	No prior smoking history or family history of lung cancer	Chest CT	f/u imaging	Resolved; most likely benign	Yes	Continued
30	F	Black	Fibroid	Denies excessive pain with menstrual cycles or heavy bleeding	f/u PET/CT imaging or pelvic ultrasound	f/u imaging	Fibroids	Yes	Continued
30	M	White	Lymphoma, adenosis in nasopharynx/ oropharynx	N/A	Endoscopy	Endoscopy	Unknown (lost to f/u)	No	Discontinued
31	F	Black	Underlying inflammation; right palatine tonsil, nonspecific	Eyes, ears, nose, mouth, and throat examination: negative result	f/u PET/CT imaging	f/u imaging	Unchanged; nonspecific	Yes	Continued
31	M	Hispanic White	Lung neoplasm in left hemithorax	N/A	f/u PET/CT imaging, chest CT, chest MRI, or tissue sampling	Unknown	Unknown (lost to f/u)	No	Discontinued
34	M	Unknown	Inflammation of cervical lymph node, nonspecific	N/A	f/u PET/CT imaging	f/u imaging	Unchanged; nonspecific most likely inflammatory	Yes	Continued
38	M	Hispanic White	Cirrhosis	Consumed 2 drinks daily	Clinical and/or laboratory correlation	f/u with PCP	Cirrhosis	Yes	Continued
39	M	Unknown	Pulmonary nodule	N/A	r/u PET/CT imaging or Chest CT	f/u imaging	nonspecific	Yes	Continued
42	F	White	Ovarian neoplasm (complex left ovarian cyst with inflammation, endometrioma)	Family history of breast and fallopian tube cancer	Pelvic MRI	Elective bilateral salpingo-oopherectomy	Ovarian cyst	Yes	Continued
43	F	Black	Superior cerebellar cistern (or arachnoid cyst)	N/A	Clinical correlation and/or brain MRI	None	Resolved	Yes	Continued
48	M	Hispanic White	Pulmonary nodule	N/A	Chest CT	f/u with specialist; chest CT	Latent TB	Yes	Continued

48	M	White	Tibial sclerosis	N/A	f/u PET/CT imaging	f/u imaging	Unchanged; most likely benign	Yes	Continued
48	M	Hispanic White	Renal Mass	N/A	Abdominal ultrasonography or MRI	f/u with PCP	Unknown (lost to f/u)	Yes	Continued
48	M	White	Small hiatal hernia	GERD intermittently, managed by diet and Tums as needed. Never Smoker.	Upper endoscopy or esophagography	Upper endoscopy	Barrett's esophagus; resolved with medication	Yes	Continued
49	M	White	Mosaic attenuation of the lungs	Smoker	Chest CT	f/u imaging	Not malignant or infectious	Yes	Continued
50	M	White	Rectal neoplasm	N/A	f/u PET/CT imaging or pelvic MRI or colonoscopy	Unknown	Unknown (lost to f/u)	Yes	Continued
51	M	White	Distal esophagus uptake, nonspecific	N/A	Upper endoscopy	Upper endoscopy	GERD	Yes	Continued
53	M	White	Colorectal carcinoma	N/A	Colonoscopy	Unknown	Unknown (lost to f/u)	No	Discontinued
53	F	Hispanic White	Sigmoid colon adenoma or carcinoma	N/A	Colonoscopy	colonoscopy	Benign adenoma	Yes	Continued
54	M	White	Prostatitis	Normal annual physical exam	Serum PSA levels	f/u with PCP	f/u with PCP	Yes	Continued
60	F	White	Pulmonary nodule and emphysema	N/A	Chest CT	f/u imaging; f/u with pulmonologist	Unchanged; most likely benign	Yes	Continued
62	M	White	Colonic polyp	Colitis (proctitis) episode previously	Colonoscopy	Seen by gastrointestinal specialist	Benign	No	Discontinued
64	M	White	Mediastinal tumor - lymphoma, thymoma, or germ cell tumor	GERD	Biopsy	Biopsy	Thymoma	No	Discontinued
68	F	White	Colonic polyp	No family history of colon cancer	Colonoscopy	f/u with gastroenterology	Unknown (lost to f/u)	Yes	Continued
75	M	White	Primary malignancy or large colonic polyp	N/A	Colonoscopy	Unknown	Unknown (lost to f/u)	No	Discontinued

All patients were asymptomatic at presentation.
ALK, ALK receptor tyrosine kinase; *CT*, computed tomography; *EFGR*, epidermal growth factor receptor; *F*, female; *f/u*, follow-up; *GERD*, gastroesophageal reflux disease; *GIST*, gastrointestinal stromal tumor; *KIT*, proto-oncogene receptor tyrosine kinase; *M*, male; *MRI*, magnetic resonance imaging; *N/A*, not applicable; *PCP*, primary care physician; *PET*, positron emission tomography; *PSA*, prostate-specific antigen; *SCC*, squamous cell carcinoma; *TB*, tuberculosis.
*Randomized and received active therapy or placebo.
†Study course: continued means continued on study protocol and discontinued means discontinued or withdrew from study protocol.

oropharyngeal adenocarcinoma, uterine leiomyosarcoma, lymphoma, and papillary thyroid carcinoma) may not have been detected on the basis of current cancer screening recommendations.

In a survey of healthy research volunteers,[18] most individuals reported a desire to be informed if clinically significant health-related research findings were discovered and their likelihood of discovery of such findings, despite the potential medical, insurance, and employment implications. Our results provide a foundation for clinical trialists to help guide the discussion during the informed consent process on what otherwise healthy patients with moderate-to-severe psoriasis can expect (ie, frequency of incidentalomas) should any clinically significant incidentalomas be found if they are undergoing comprehensive radiologic imaging during a clinical trial.

Though there are differing views on the handling of incidentalomas,[10,19] we encourage clinicians and researchers to develop procedures that are suitable within their framework, such as collaborating with local hospitals or conferring with other specialists for further evaluation and management (ie, developing a procedure to disclose findings to patients and discussions of next steps). As part of our process, we developed a systematic procedure for managing clinically significant incidentalomas whereby we internally track and discuss clinically significant incidentalomas within our research team, which includes a radiologist, and subsequently relay information to the patient and to the relevant clinical service in a timely manner. Several research bodies and teams have reported different methods of managing incidentalomas,[20] such as incorporating a dedicated section in the electronic medical record to signal whether an incidentaloma was found[21] or creating a closed feedback loop with the patients' research team and primary care physician.[22,23]

Our findings can also be used to inform interpretation of safety data on novel therapies, as there are numerous reports of malignancy in clinical trials of immune-modulating treatments for psoriasis.[24] For example, in a phase 3 trial of 666 patients with moderate-to-severe plaque psoriasis who were receiving tofacitinib, 3 patients had malignancies: colon cancer (59 days after initiation), prostate cancer (84 days after initiation), and pancreatic cancer (138 days after initiation).[25] Given the statistical rarity of cancer, investigators, regulators, and others may falsely interpret a safety signal when cancers are observed in a clinical trial. However, our data provide an estimate of what the prevalence rate of cancer is in the population with moderate-to-severe psoriasis and therefore should help inform interpretation of these safety results.

As with all studies, there are limitations to consider. These results may not be generalizable to the non-US population of patients with moderate-to-severe psoriasis. However, our patients' characteristics (age, sex, duration of psoriasis, and PASI score) are quite similar to those of most large phase 3 programs and thus are likely generalizable to the US population. The clinical trial population may falsely inflate signals discovered through imaging, as it may include uninsured individuals who have limited access to health care and therefore may have prior undiagnosed diseases.[26]

CONCLUSION

In summary, clinically significant findings on FDG PET/CT imaging are common in otherwise healthy asymptomatic patients with moderate-to-severe psoriasis who are participating in clinical trials. Of special importance is the fact that at least 2.3% of patients had serious unrecognized cancers. These findings can help inform the interpretation of safety data from clinical trials and further emphasize the importance of encouraging patients with moderate-to-severe psoriasis to be compliant with current, age-appropriate cancer screening recommendations.

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