1.0 Abstract

Title

A non-interventional prospective cohort study to provide real-world evidence on the treatment goal achievement rate, adherence to and utilization patterns of adalimumab in patients with moderate to severe plaque psoriasis in Greece-CONCORDIA STUDY

Keywords

adalimumab, DLQI, PASI, patient adherence, plaque psoriasis, quality of life, treatment success

Rationale and Background

Taking into consideration the recent advent of the Progressive Psoriasis Initiative (PPI) recommendations in conjunction with the European Consensus Programme (ECP) definitions of moderate to severe psoriasis and treatment goals as well as the scarcity of real-world evidence on the implementation and impact of these guidelines, it was considered of great interest to assess the outcomes of treatment with adalimumab from the perspective of the well-defined, widely-accepted and consensus-guided disease severity and treatment success definitions as well as drug utilization practice recommendations, among moderate to severe psoriasis patients treated in routine clinical practice settings in Greece.

Research Question and Objectives

The primary objective of the study was to assess the treatment goal achievement rate at the induction phase completion (i.e., 16 weeks post-baseline), according to the ECP-defined criteria.

Secondary objectives

- To assess the ECP-defined treatment goal achievement rate at 6, 8, and 12 months after adalimumab treatment onset among the overall study population

- To assess the ECP-defined treatment success, intermediate response, and treatment failure rates at 16 weeks, and at 6, 8, and 12 months after adalimumab treatment onset among the overall study population

- To depict patterns of transitioning from a prior conventional systemic or biologic agent to treatment with adalimumab and the agreement with PPI recommendations, among patients who have previously received systemic therapy

- To assess adalimumab utilization patterns in routine clinical practice and their agreement with PPI recommendations in terms of treatment modifications, the addition of another therapeutic modality to adalimumab treatment along with the reasons for these modifications, among the overall population throughout the study observation period

- To record patients' adherence and persistence to treatment with adalimumab during the study observation period, as well as the reasons for missed doses and time to the first missed dose

- To estimate the impact of adalimumab treatment on patients' quality of life, as measured by Dermatology Life Quality Index (DLQI) at each post-baseline study timepoint among the overall population, as well as in the subpopulations achieving treatment success, intermediate response, and treatment failure

- To estimate the impact of adalimumab treatment on disease severity as measured by Psoriasis Area Severity Index (PASI) at each post-baseline study timepoint among the overall population

- To evaluate the frequency of offering the option and participating in a Patient Support Program (PSP) at the time of initiating adalimumab treatment, as well as to document the reasons for not offering the option or not participating in the PSP

- To examine potential factors associated with the achievement of the treatment goal at the completion of the induction phase, as well as at the end of study observation period

Study Design

This was a post-marketing, multicenter, observational study including patients with moderate to severe plaque psoriasis treated with adalimumab in real-life clinical settings in Greece. The overall study duration period was expected to be 24 months, including a 12-month recruitment period and a 12-month follow-up period. Study-related information was collected at baseline (prior or at the time of adalimumab treatment onset) and at 4 post-baseline timepoints: 16 weeks (±1 week) and 6, 8 and 12 months (±2 weeks) post adalimumab treatment onset. Patients were followed until the end of the 12-month observation period or until death, consent withdrawal, unacceptable toxicity or physician's decision to discontinue the patient from the study, or adalimumab treatment discontinuation for any reason other than achievement of treatment goals, whichever occurred earlier.

Setting

The study was planned to be conducted across approximately 60 sites in Greece (comprising both hospital- and office-based physicians), under routine clinical practice.

Patients and Study Size, Including Dropouts

A total of 281 patients meeting all the below-mentioned inclusion criteria and none of the exclusion criteria were enrolled in the study.

Inclusion criteria: 1) male and female ≥18 years of age; 2) clinical diagnosis of plaque psoriasis for at least 6 months, and moderate to severe disease course at the time of adalimumab treatment onset, defined as body surface area (BSA) >10 or PASI >10 and DLQI >10; 3) patients for whom the decision to prescribe therapy with adalimumab (Humira®) according to the locally approved summary of product

characteristics (SmPC) was already taken prior to their enrollment in the study and was clearly separated from the physician's decision to include the patient in the current study; 4) available PASI and DLQI scores at the start of adalimumab treatment; 5) able and willing to provide written informed consent and to comply with the requirements of the study protocol; 6) signed informed consent document.

Exclusion criteria: 1) non-plaque forms of psoriasis (e.g., erythrodermic, guttate, or pustular); 2) treatment with adalimumab initiated more than 2 weeks prior to their enrollment into the study; 3) contraindications to the administration of the study drug according to the latest version of the locally approved SmPC; 4) previous exposure to adalimumab, unless a period of at least 6 months from the last dose elapsed; 5) current treatment with any investigational drug/device/intervention or receipt of any investigational product within 1 month or 5 half-lives of the investigational agent (whichever is longer) before the commencement of therapy with adalimumab.

Drop-outs: Overall, 36 patients (12.8%) prematurely discontinued study participation after a median of 5.1 months post-adalimumab treatment onset. Reasons for premature premature discontinuation of study participation are presented in the results section below.

Variables and Data Sources

The study mainly involved primary data collection, by means of a web-based data capture system that adhered to all applicable data protection regulations and requirements with regard to electronic records. In accordance to the study's non-interventional design, primary data collection was mainly employed. Data were mainly collected prospectively during the study visits through patients' interview and patient reported outcomes (PROs; DLQI).

The variables pertaining to the primary endpoint included the patients' baseline and Week 16 PASI score and the DLQI score at Week 16 (end of the induction phase). Variables pertaining to secondary endpoints included patient and disease

characteristics at baseline, prior therapies, PASI and DLQI scores at enrolment and at the Week 16, Month 6, Month 8 and Month 12 post-baseline timepoints, the patients' transitioning strategy employed and agreement with the PPI recommendations regarding the length of washout and reasons for implementing a washout or not according to the type of immediately prior systemic therapy; modifications in the dosing interval and/or dose and treatment interruption(s), along with the reasons for each modification/adjustment; adalimumab administration characteristics (i.e. monotherapy or combination therapy, changes throughout the study observation period, date of discontinuation, date of first missed dose, number of missed doses, number of prescribed doses); patients offered the option of PSP participation at the time of initiating adalimumab and reasons for not offering this option from the physician's side, as well as reasons for not participating among patients who were offered the option to participate.

Results

Overall, 281 eligible patients were enrolled in the study over an approximate 22-month recruitment period (between 16-June-2016 [FPFV] and 26-April-2018 [LPFV]), by dermatology specialists practicing in 42 participating sites (10 hospitals and 32 private practices) located across 8 administrative regions in Greece. The overall study duration was 34.2 months (from FPFV to LPLV [24-April-2019]). Among the eligible patients, 48.4% (136/281) were enrolled by 19 sites located in Attica, and 51.6% (145/281) by 23 sites located outside Attica.

The median duration of patients' follow-up in the context of the study was 11.8 months. Overall, 36 patients (12.8%) prematurely discontinued study participation after a median of 5.1 months post-adalimumab treatment onset, due to "adalimumab treatment discontinuation" in 61.1% (22/36) and "loss to follow-up" in 38.9% (14/36) of the patients.

Baseline patient and disease characteristics

Among eligible patients, 98.2% (276/281) were Caucasian, and 61.9% (174/281) were males. At enrollment, the patients' mean age was 49.0 years, and the median BMI was 26.6 kg/m^2, with 43.4% (122/281) of the patients classified as overweight, and 25.6% (72/281) as obese. In addition, 57.7% (162/281) of the patients were ever-smokers [29.2% (82/281) were current, 17.1% (48/281) occasional, and 11.4% (32/281) were former smokers].

The median age of the patients at psoriasis signs and symptoms onset and at disease diagnosis was 35.6 and 36.4 years, respectively. At initial diagnosis, the severity of psoriasis was moderate-to-severe in 65.5% (173/264) of the evaluable patients. A family history of psoriasis and psoriatic arthritis was reported for 36.3% (89/245) and 7.3% (17/233) of the evaluable patients, respectively.

At adalimumab treatment onset (baseline), 76.5% (215/281) of the patients had psoriatic scalp manifestations, 48.8% (137/281) had nail involvement, 37.4% (105/281) had palmoplantar involvement, and 15.9% (43/270) of evaluable patients had psoriatic arthritis. The median baseline BSA, PASI and DLQI scores were 30.0%, 16.5, and 15.0, respectively.

At baseline, at least one past or ongoing clinically significant medical condition/comorbidity was reported for 22.8% (64/281) of the patients, with those reported for ≥5% of the patients being 'hypertension' (11.4%; 32/281) and 'hyperlipidaemia/dyslipidaemia/hypercholesterolaemia' (7.5%; 21/281).

Prior systemic therapy and adalimumab treatment characteristics

At adalimumab treatment onset, 55.5% (156/281) of the patients had been exposed to prior systemic treatment for psoriasis. The immediately prior systemic therapy included non-biologic therapy only for 38.1% (107/281), biologic therapy only for 15.7% (44/281), and both biologic and non-biologic in 1.8% (5/281). Biologics included etanercept (6.0%; 17/281), ustekinumab (4.6%; 13/281), infliximab (4.3%; 12/281), adalimumab (1.4%; 4/281), secukinumab (0.7%; 2/281), and certolizumab pegol (0.4%; 1/281). Non-biologic treatments included cyclosporine (19.9%; 56/281), apremilast (8.5%; 24/281), methotrexate (6.4%; 18/281), acitretin (5.0%; 14/281), and

leflunomide (0.4%; 1/281). The immediately prior systemic therapy had been discontinued a median of 2.11 months before adalimumab onset for 150 patients *[1.77 months for the non-biologics and 2.75 months for the biologics]*, whereas for six patients prior systemic therapy overlapped with adalimumab.

Among patients previously exposed to systemic therapy (N=156), a transition (switching or overlapping) strategy to adalimumab was not applicable for 79 patients (64 patients previously treated with non-biologics and 15 patients previously treated with biologics) due to a long period elapsed from previous treatment discontinuation to adalimumab onset. Therefore, a transitioning strategy was applicable for 77 patients including 43 patients that had previously received non-biologic systemic therapy, and 34 patients that had previously received biologic systemic therapy (with or without non-biologic therapy). Among patients who transitioned to adalimumab from non-biologic systemic therapy (N=43), 55.8% (24/43) switched therapy following a washout period, 30.2% (13/43) switched therapy without a washout period, and 14.0% (6/43) had an overlap between the two treatments. Among patients who transitioned from biologic therapy (with or without non-biologic systemic therapy; N=34), 41.2% (14/34) switched biologic therapy to adalimumab following a washout period, and 58.8% (20/34) switched therapy without a washout period.

Physician's compliance with PPI recommendations regarding the transitioning from a prior systemic treatment (biologic or non-biologic) to adalimumab was noted for 88.2% (67/76) of evaluable patients for whom a transitioning strategy was applicable. This rate was 90.7% (39/43) for patients transitioning from a non-biologic and 84.8% (28/33) for those transitioning from biologic therapy.

All patients were newly initiated on treatment with adalimumab as per the locally approved SmPC. The patients' mean age at adalimumab treatment onset was 49.0 years with a median of 7.9 years having being elapsed since psoriasis diagnosis. The median adalimumab treatment duration in the context of the study was 11.7 months. Adalimumab was initiated as monotherapy in 96.4% (271/281) and as combination therapy in 3.6% (10/281) of the patients. Concomitant systemic therapy for psoriasis was received by 7.1% (20/281) of the patients at any time during the study observation

period, and included cyclosporine in 10 patients (3.6%), methotrexate in 9 patients (3.2%), acitretin in 2 patients (0.7%), and leflunomide in one patient (0.4%). None of the patients received phototherapy during the study observation period.

Over the study observation period, a total of 20 modifications in adalimumab dosing frequency (17 increases and 3 decreases in dosing frequency) were recorded for 6.4% (18/281) of the patients, including dose intensification (from 40 mg every 2 weeks to 40 mg weekly) in 16 patients (5.7%) due to inadequate therapeutic response *(in a single patient the dosing frequency returned to 40 mg every 2 weeks after achievement of response)*, and dose de-escalation (from 40 mg every 2 weeks to 40 mg every 3 weeks) in 2 patients due to patient's wish *(in this patient the dosing frequency returned to 40 mg every 2 weeks)* and achievement of therapeutic response. Moreover, 7 treatment temporary interruptions were recorded for 2.5% (7/281) of the patients due to patient's decision (in 3 patients), AE occurrence (in 3 patients), and achievement of therapeutic response (in one patient). Overall, 24 patients (8.5%) permanently discontinued adalimumab after a mean of 22.5 weeks post-treatment onset, due to lack of therapeutic effectiveness (in 13 patients), patient's decision/wish (in 7 patients), AE occurrence (in 3 patients), and physician's decision to change therapy (in one patient). Ten patients (3.6%) discontinued treatment by the end of the 16-week induction phase, and 14 patients (5.0%) discontinued treatment after the completion of the induction phase.

Regarding treatment adherence during the study observation period, 7.5% (19/255) of the evaluable patients missed at least one adalimumab injection with a mean time elapsed from adalimumab treatment onset to first missed injection of 4.8 months. Considering patients with known total number of missed adalimumab injections (N=245), 9 patients missed a total of 41 adalimumab injections (median of 2.0 injections) due to patient's wish/decision (25 injections by 5 patients), patient's neglect (3 injections by 2 patients), delay in prescription renewal (1 injection by 1 patient), insufficient response (4 injections by 1 patient) and for unknown reason (8 injections by 1 patient).

Overall, 95.4% (268/281) of the patients in the overall population were offered by the physicians the option to participate in the PSP for adalimumab at any time during the study observation period *[79.4% (223/281) were offered this option at adalimumab treatment onset and 16.0% (45/281) post-adalimumab treatment onset]*; the most frequent reasons for not offering this option to the remaining 4.6% (13/281) of the patients were physician-perceived lack of benefit for the patients, and inadequate information about the program. During the study observation period, 15.7% (42/268) of the patients who were offered the option to participate in the PSP actually participated in the PSP. Among those who were offered this option but did not finally participate in the PSP (84.3%; 226/268), the reported reasons were '*patient's refusal/not interested/not needed*' (64.2%; 145/226), '*support offered by pharmacist/physician/family member*' (4.9%; 11/226), both aforementioned reasons (7.1%; 16/226), other *(personal reasons/lack of time/inability to participate)* (4.4%; 10/226), and unknown/missing (19.5%; 44/226).

Achievement of the ECP-defined treatment goals

Based on the NRI method, **57.7%** (162/281; 95% CI: 51.9-63.4) of the patients achieved the **ECP-defined treatment goal** *[i.e., treatment success (≥75% PASI reduction) or intermediate response (PASI reduction ≥50% but <75%) with DLQI ≤5]* at the end of the **16-week** induction phase; the respective as-observed 16-week goal attainment rate was **62.1%** (162/261; 95% CI: 56.2-68.0). At **6**, **8**, and **12 months** post-adalimumab onset, the treatment goal attainment rate (based on the as observed data) was **88.4%** (221/250), **94.8%** (239/252), and **95.5%** (233/244), respectively, among the evaluable patients. According to the last available post-baseline assessment for each patient, i.e. at the **end of each patient's observation**, the goal achievement rate among patients with available data was **90.5%** (248/274; 95% CI: 87.0-94.0).

The **treatment success rates** (i.e., PASI score reduction ≥75%) (based on the as observed data) at **16 weeks**, and at **6**, **8**, and **12 months** post-baseline were **53.6%** (140/261), **81.6%** (204/250), **90.1%** (227/252), and **92.2%** (225/244), respectively; the relevant rate at the **end of observation** was **87.6%** (240/274).

The **intermediate response rates** (i.e., PASI score reduction ≥50% but <75%) **with DLQI ≤5** at **16 weeks**, and at **6**, **8**, and **12 months** post-baseline were **8.4%** (22/261), 6.8% (17/250), **4.8%** (12/252), and **3.3%** (8/244), respectively; the relevant rate at the **end of observation** was **2.9%** (8/274). The **intermediate response rates** (i.e., PASI score reduction ≥50% but <75%) **with DLQI >5** at **16 weeks**, and at **6**, **8**, and **12 months** post-baseline were **13.4%** (35/261), **4.8%** (12/250), **2.4%** (6/252), and **1.6%** (4/244), respectively; the relevant rate at the **end of observation** was **2.9%** (8/274). The **treatment failure rates** (i.e., PASI score reduction <50%) at **16 weeks**, and at **6**, **8**, and **12 months** post-baseline were **24.5%** (64/261), **6.8%** (17/250), **2.8%** (7/252), and **2.9%** (7/244), respectively; the treatment failure rate at the **end of observation** was **6.6%** (18/274).

Change in DLQI score throughout the study observation period

In the **overall population**, among patients with paired data, the median total DLQI score decreased from **15.0** at baseline to **5.0** at **Week 16** post-baseline [significant decrease of a median of 11.0 points (p<0.001)]. Moreover, the median total DLQI score decreased from **15.0** at baseline to **2.0** at **Month 6** post-baseline, from **15.0** at baseline to **1.0** at **Month 8**, and from **14.0** at baseline to **0.0** at **Month 12**, representing significant decreases of a median of 12.0, 13.0, and 13.0 points, respectively (p<0.001 for all). Significant decreases were also noted in all DLQI domain scores between baseline and all post-baseline timepoints (p<0.001 for all).

Among evaluable patients with **treatment success** at the **end of the induction phase**, the median total DLQI score decreased from **15.0** at baseline to **2.0** at **Week 16** [significant decrease of a median of 12.0 points (p<0.001)]. In addition, among evaluable patients with **treatment success** at the **end of observation**, the median total DLQI score decreased from **15.0** at baseline to **2.0** at **Month 6**, from **15.0** at baseline to **1.0** at **Month 8**, and from **14.0** at baseline to **0.0** at **Month 12**, representing significant decreases of a median of 12.0, 13.0, and 13.0 points, respectively (p<0.001 for all). Significant decreases were also noted in all DLQI domain scores between baseline and all post-baseline timepoints (p<0.001 for all).

Among evaluable patients with **intermediate treatment response** (i.e. with PASI reduction ≥50% but <75% regardless of DLQI) at the **end of the induction phase**, the median total DLQI score decreased from **15.0** at baseline to **7.0** at **Week 16**, representing a statistically significant decrease of a median of 9.0 points (p<0.001). In addition, among evaluable patients with intermediate treatment response at the **end of observation**, the total DLQI score significantly decreased at all post-baseline timepoints (p<0.001 for all).

Among evaluable patients with **treatment failure** (i.e. PASI reduction <50%) at the **end of the induction** phase, the median total DLQI score decreased from **13.0** at baseline to **9.0** at **Week 16** [significant decrease of a median of 5.0 points (p<0.001)]. In addition, among evaluable patients with treatment failure at the **end of observation**, significant improvements in the total DLQI score were noted at **Month 6** (p<0.001) and **Month 8** (p=0.006) post-baseline; no statistical comparisons were performed in the change in the DLQI score from baseline at Month 12 due to the small number of patients with available paired data.

Change in PASI score throughout the study observation period

Among patients in the **overall population** with paired data, the median total PASI score decreased from **16.5** at baseline to **3.9** at **Week 16**, from **16.5** at baseline to **1.8** at **Month 6**, from **16.7** at baseline to **1.0** at **Month 8**, and from **16.8** at baseline to **0.6** at **Month 12** post-baseline. These changes represented significant decreases in the total PASI score of a median of 11.7 points at Week 16, 14.4 points at Month 6, 15.0 points at Month 8, and 15.6 points at Month 12 (p<0.001 for all). Significant percent decreases from baseline were also noted at all post-baseline timepoints (p <0.001 for all); specifically, the median percent decreases were 75.9%, 90.0%, 94.7%, and 96.7% at Week 16, Month 6, Month 8, and Month 12 post-baseline, respectively (p <0.001 for all). Statistically significant absolute and percent decreases (p <0.001 for all) were noted in all PASI domain scores between baseline and all post-baseline timepoints.

The associations of selected baseline patient, disease, and treatment characteristics *(i.e., age, sex, BMI, active smoking, presence of comorbidities, psoriasis duration, age*

at psoriasis diagnosis, psoriatic arthritis, DLQI, PASI, nail involvement, scalp involvement, palmoplantar involvement, prior systemic treatment, and prior biologic systemic treatment) with the ECP-defined treatment goal achievement at completion of the induction phase and at the end of the study observation period were examined through univariable and multivariable logistic regression models using the as observed data.

In regard to the association of various factors of interest with the achievement of the ECP-defined treatment goal **at the end of induction phase**, the following significant associations were demonstrated by the multivariable analysis:

- **Baseline BMI**: Patients with baseline BMI≥30 kg/m^2 had 49% lower odds of achieving the treatment goal than patients with BMI<30 kg/m^2 (OR: 0.51; p=0.029).
- **Baseline PASI**: Every one-unit increase in baseline PASI was associated with 3% increase in the odds of achieving the treatment goal (OR: 1.03; p=0.018).
- **Scalp involvement at baseline**: Patients with versus those without scalp involvement at baseline had approximately 2.4 times higher odds of achieving the treatment goal (OR: 2.42; p=0.005).

As regards the association of various factors of interest with the achievement of the ECP-defined treatment goal at the **end of the study observation** period, the following significant associations were demonstrated by the multivariable analysis:

- **Baseline BMI**: Patients with BMI≥30 kg/m^2 at baseline had 60% lower odds of achieving the treatment goal than patients with BMI<30 kg/m^2 (OR: 0.40; p=0.043).
- **Baseline PASI**: Every one-unit increase in baseline PASI was associated with 7% increase in the odds of achieving the treatment goal (OR: 1.07; p=0.027).
- **Palmoplantar involvement**: Patients with versus those without palmoplantar involvement at baseline had approximately 4.3 times higher odds of achieving the treatment goal (OR: 4.31; p=0.023).

- **Prior systemic treatment for psoriasis**: Patients with any prior systemic treatment had 81% lower odds of achieving the treatment goal than treatment-naïve patients (OR: 0.19; p=0.004).

Safety outcomes

As per the protocol requirements, the adverse events (AEs) actively solicited in the context of 'CONCORDIA' included all serious AEs and any non-serious malignancies in patients 30 years of age and younger. No other non-serious AEs were actively solicited nor captured in the eCRF, but were to be collected as spontaneous reports if AbbVie was notified. Specific questioning at each study visit in the eCRF ensured that physicians were aware of these reporting requirements and the clinical study monitor further inquired about the occurrence of any such events and checked the patients' source data (medical records) during the on-site monitoring visits as means to avoid any under-reporting of such AEs.

In total, 3 serious AEs related to adalimumab (ADRs; "folliculitis" in one patient and "dyspnoea" and "malaise" in another patient) were reported for 2 patients (1.4%); all three events led to permanent treatment discontinuation and all had recovered by the end of safety follow-up period. No cases of malignancies in patients ≤30 years of age were recorded.

Discussion

The study provides real-world evidence on the effect of adalimumab on ECP-defined treatment goal achievement, disease severity and patients' dermatology-specific QoL, at the end of the induction phase and over a 12-month observation period in patients with moderate to severe psoriasis treated with adalimumab in the routine care setting in Greece. Moreover, the study has provided insight into the real-life drug utilisation patterns and transitioning strategies employed when initiating adalimumab along with their agreement with the PPI recommendations, and into patients' adherence and persistence to therapy and utilization of the PSP for adalimumab. The study indicates the beneficial impact of adalimumab on PASI and DLQI outcomes leading to about 6 in 10 patients achieving the treatment goal at 16 weeks, with this rate increasing over

time through 12 months. Positive predictive baseline factors for treatment response at 16 weeks post-treatment onset included non-obesity, higher PASI and presence of psoriatic nail manifestations, whereas the baseline factors predicting response to adalimumab treatment at 12 months were non-obesity, higher PASI, presence of palmoplantar manifestations and exposure to prior systemic therapy for psoriasis. Physicians' compliance with PPI recommendations regarding the transitioning from a prior systemic treatment to adalimumab was noted for about 9 in 10 patients for whom a transitioning strategy was applicable. In addition, the study demonstrated a high 12-month drug survival rate and patients' adherence to treatment, both exceeding 90%, albeit the rate of participation in the PSP was low (with fewer than 2 in 10 patients participating) even though this option was offered to the vast majority of the patients.

The eligible study population was enrolled from sites located across 8 of the 13 administrative regions of Greece, which are home to approximately 87% of the overall Greek population, with 48.4% enrolled by 19 sites located in Attica, the most populous region in Greece (residence to 35% of the overall Greek population). This geographic diversity of the sites enhances generalizability of the outcomes. Moreover, representativeness was facilitated by the enrollment of patients by 42 public/private hospital- and office-based physicians specializing in dermatology, allowing for reflection of variations in medical practice paradigms.

Marketing Authorisation Holder(s)

Abbvie Pharmaceuticals S.A. (Greece)

Names and Affiliations of Principal Investigators

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