Supplementary Tables and Figures

Targeted Therapy and Chemotherapy Associated Skin Toxicity: Systematic Review and Meta-analysis

Research Questions and scope of work:

Q2. Treatment of Skin Effects from Cancer Treatment with EGFR inhibitors

Population	**Intervention(s)**	**Comparator**	**Patient Important Outcomes**
Patients on EGFR inhibitors (rash prevention)	Oral antibiotics (doxycycline or minicycline)	Usual care (skin care regimen – sunscreen, mild cleanser, moisturizer cream)	Quality of life Development of acneiform rash Pruritis Adverse events from intervention Time to development of rash
Patients on EGFR inhibitors (rash prevention)	Topical steroids	Usual care (skin care regimen – sunscreen, mild cleanser, moisturizer cream)	Quality of life Development of acneiform rash Pruritis Adverse events from intervention Time to development of rash
Patients on EGFR inhibitors who have developed a grade 1/2 acneiform rash	Topical corticosteroids combined with oral antibiotics	Usual care (skin care regimen – sunscreen, mild cleanser, moisturizer cream)	Quality of life Infection Pruritis Adverse events from intervention Severity/change in rash Treatment interruption/discontinuation

Patients on EGFR inhibitors who have developed a grade 3 acneiform rash	Topical isotretinoin	Usual care (skin care regimen – sunscreen, mild cleanser, moisturizer cream)	Quality of life Infection Pruritis Adverse events from intervention Severity/change in rash Treatment interruption/discontinuation
Patients on EGFR inhibitors who have developed a grade 3 acneiform rash	Oral corticosteroids	Usual care (skin care regimen – sunscreen, mild cleanser, moisturizer cream)	Quality of life Infection Pruritis Adverse events from intervention Severity/change in rash Treatment interruption/discontinuation
Patients on EGFR inhibitors who have developed a grade 3 acneiform rash	Oral antibiotics	Usual care (skin care regimen – sunscreen, mild cleanser, moisturizer cream)	Quality of life Infection Pruritis Adverse events from intervention Severity/change in rash Treatment interruption/discontinuation

Q3. Treatment and prevention of hand foot syndrome (skin effect) of chemotherapy

Treatment			
Patients receiving infusion chemotherapy at risk for PPE (Taxane, 5FU, doxorubicin, cytarabine infusion-related HFS) PPE – palmar-plantar erythrodysesthesia (hand foot syndrome)	Cooling procedures	Best supportive care	Development of Hand Foot Syndrome Quality of life (functional limitations) Adverse events from intervention Treatment interruption/discontinuation
Patients receiving chemotherapy at risk for PPE (Taxane, 5FU, doxorubicin, cytarabine infusions plus capecitabine)	Emollient lotion	Best supportive care	Development of Hand Foot Syndrome Quality of life (functional limitations) Adverse events from intervention Treatment interruption/discontinuation
Patients receiving chemotherapy at risk for PPE (Taxane, 5FU, doxorubicin, cytarabine infusions plus capecitabine)	Pyridoxine (B6 oral)	Best supportive care	Development of Hand Foot Syndrome Quality of life (functional limitations) Adverse events from intervention Treatment interruption/discontinuation
Patients receiving chemotherapy at risk for PPE (Taxane, 5FU, doxorubicin, cytarabine infusions plus capecitabine)	Topical steroids	Best supportive care	Development of Hand Foot Syndrome Quality of life (functional limitations) Adverse events from intervention Treatment interruption/discontinuation

Prevention			
Patients receiving multikinase inhibitors (TKI, Braf – sorafenib, sunitinib, cabozantinib, regorafenib, axitinib, pazopanib, vandetanib, vemurafenib, dabrafenib) with grade 2 HFSR (Hand-foot skin reaction)	Topical urea and topical steroids (clobetasol 0.05%)	Best supportive care	Development of HFSR Quality of life (functional limitations) Adverse events from intervention Treatment interruption/discontinuation

Q4. Treatment of immunotherapy-related deep pruritis (targeted agents/PD1 inhibitors)

Patients receiving an immunotherapeutic agent who are experiencing pruritis in the absence of dermatitis	Topical corticosteroids and emollients	Best supportive care	Quality of life Adverse events from treatment Cost Time to develop pruritis

Q5. Chemotherapy-induced alopecia

Patients receiving cytotoxic agents that have the potential to cause alopecia	Cooling caps	Best supportive care	Quality of life Development of alopecia Scalp metastasis Patient comfort Adverse events from intervention Self-estimated hair loss (Dean scale)

			Cost (patient and institutional)
Patients following cytotoxic treatment who have alopecia	Rogaine	Best supportive care	Quality of life Resolution of alopecia Adverse events from intervention Self-estimated hair loss (Dean scale) Cost

Figure S1. Risk of bias assessment for randomized clinical trials

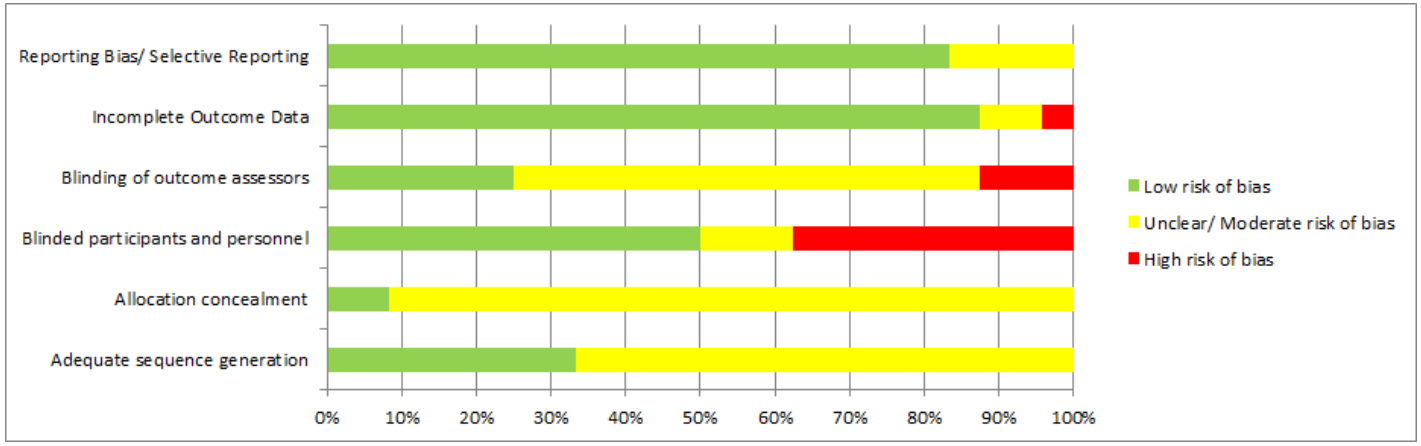

Figure S2. Risk of bias assessment for observational studies and non-randomized studies

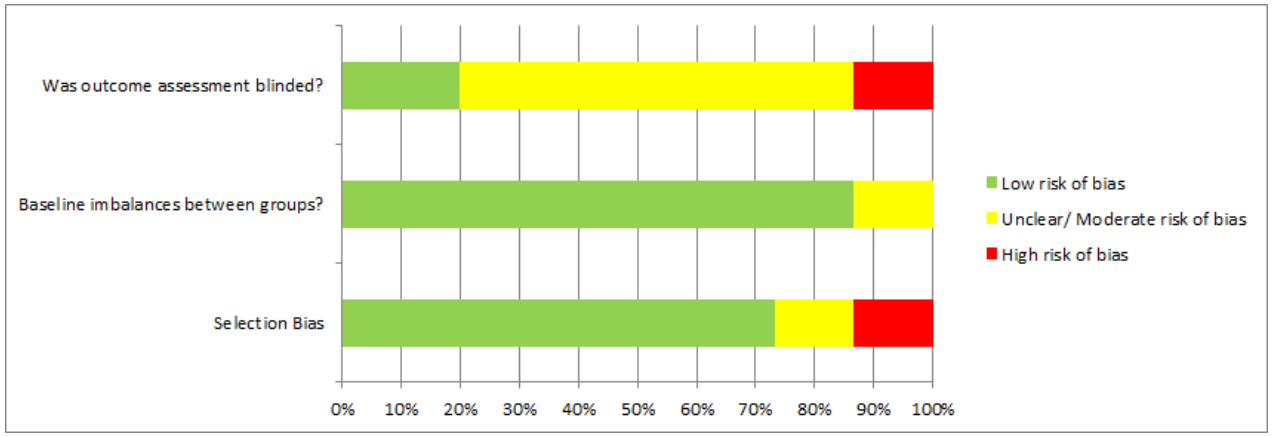

Figure S3. Risk of acneiform rash from cancer treatment with EGFR inhibitors Grade 1 (NCI-CTCAE criteria)

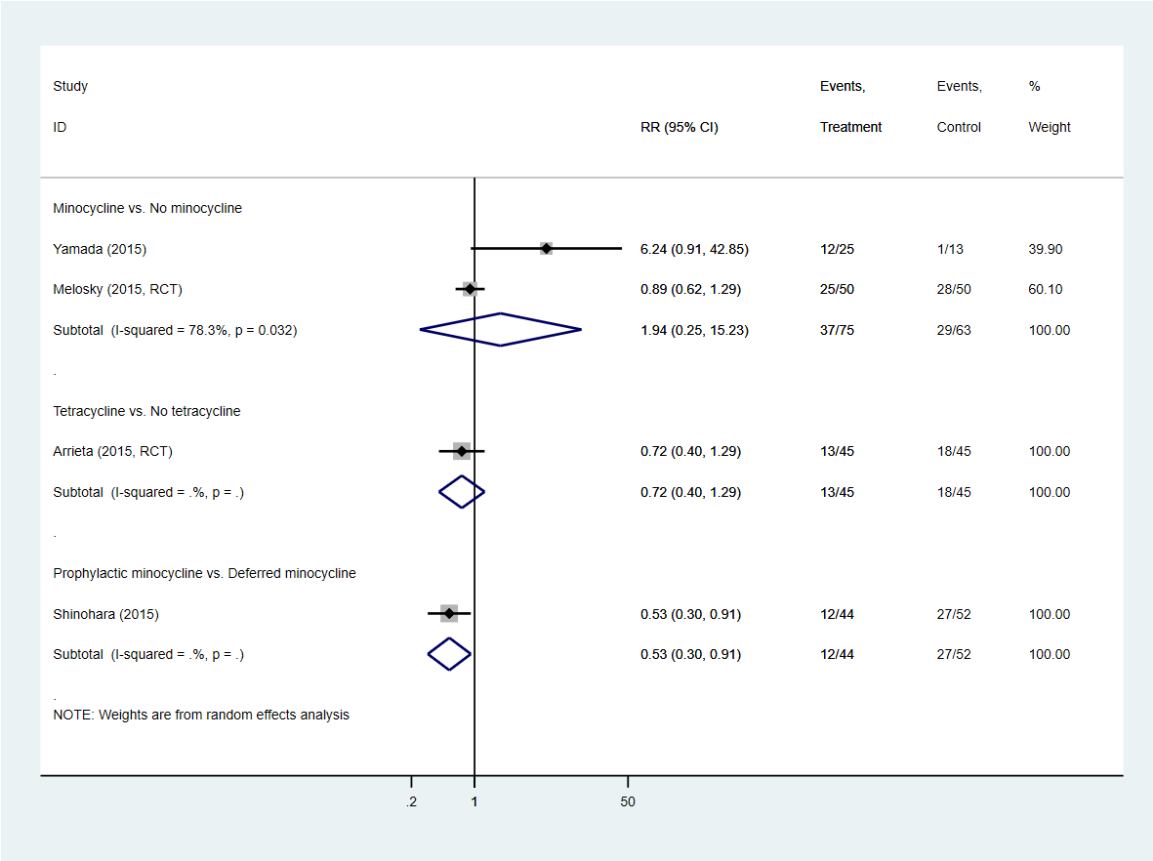

Figure S4. Risk of acneiform rash from cancer treatment with EGFR inhibitors Grade 2 (NCI-CTCAE criteria)

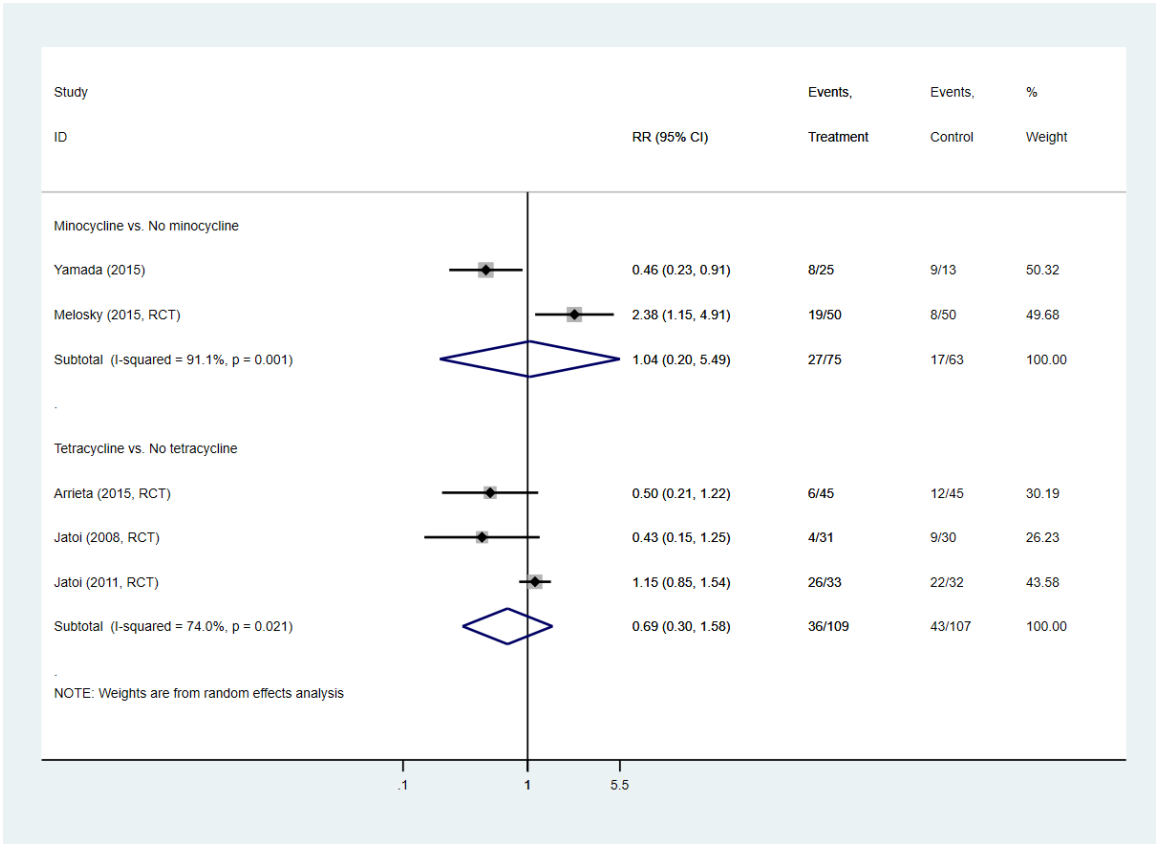

Figure S5. Risk of acneiform rash from cancer treatment with EGFR inhibitors Grade 3 (NCI-CTCAE criteria)

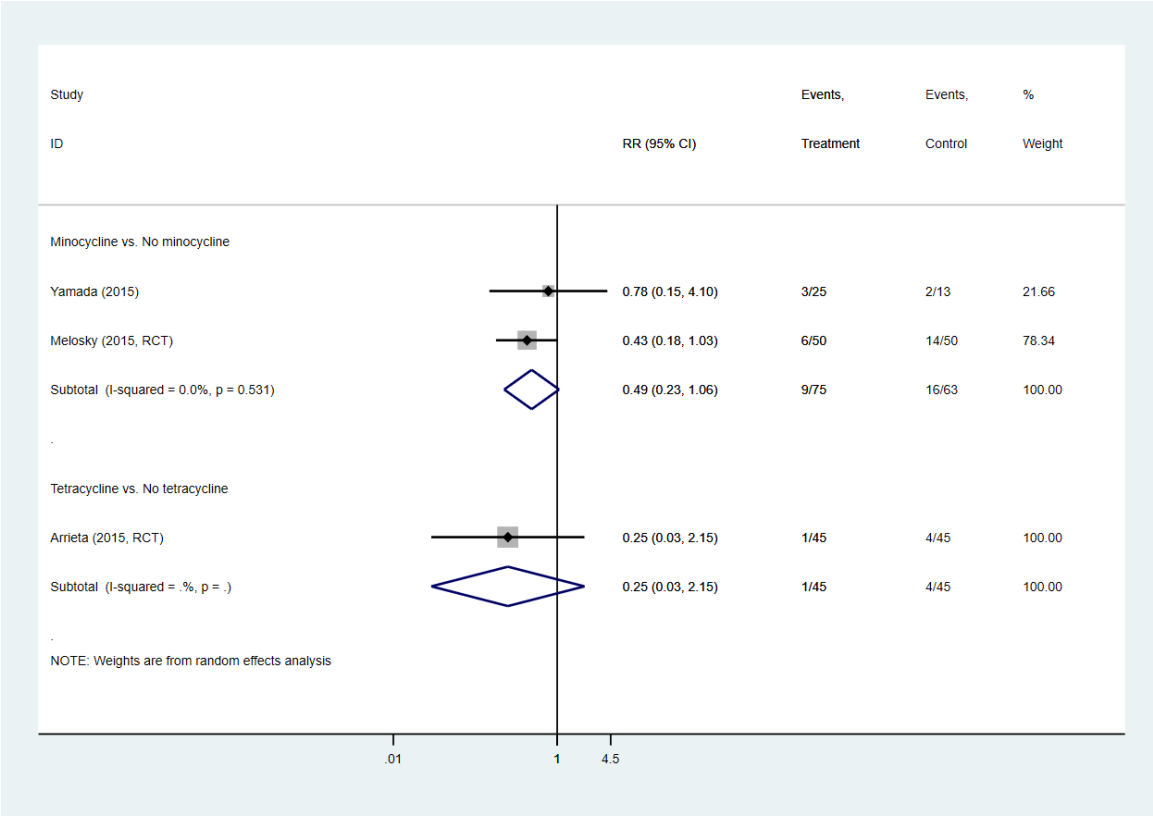

Figure S6. Risk of hand foot syndrome from chemotherapy. All grades (NCI-CTCAE criteria)

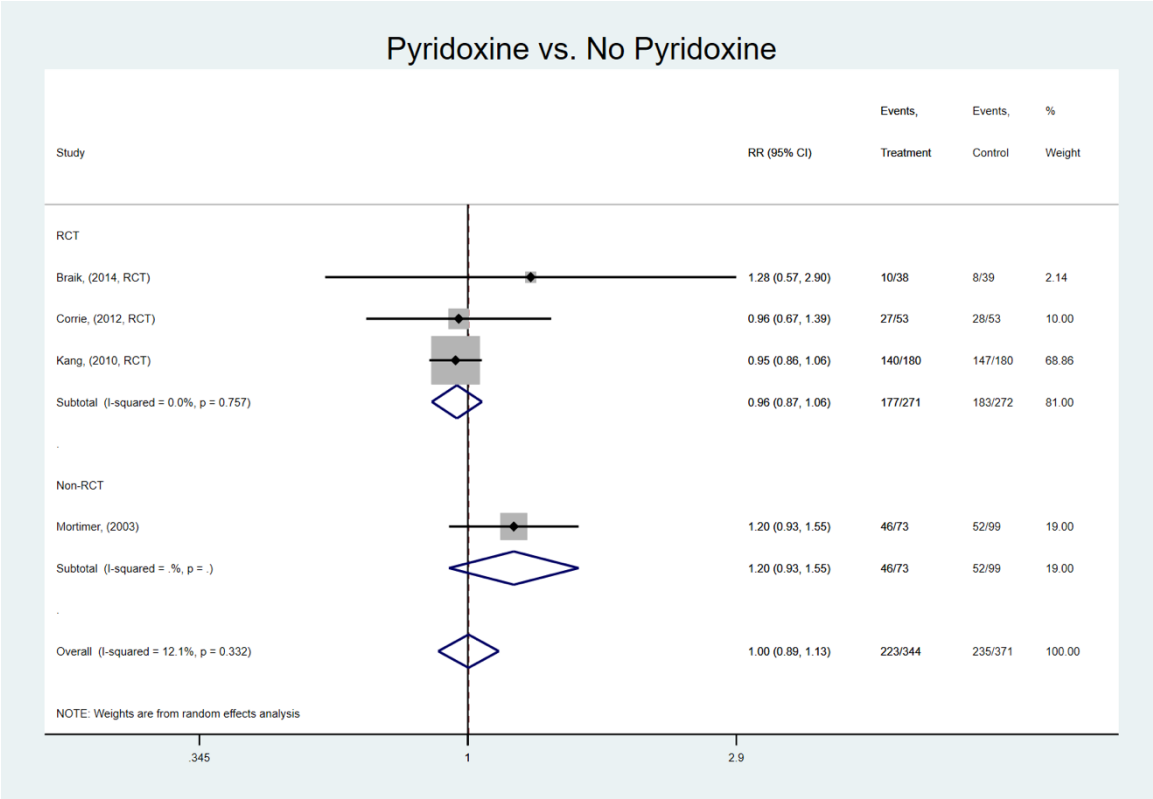

Figure S7. Risk of hand foot syndrome from chemotherapy. Grade 1 (NCI-CTCAE criteria)

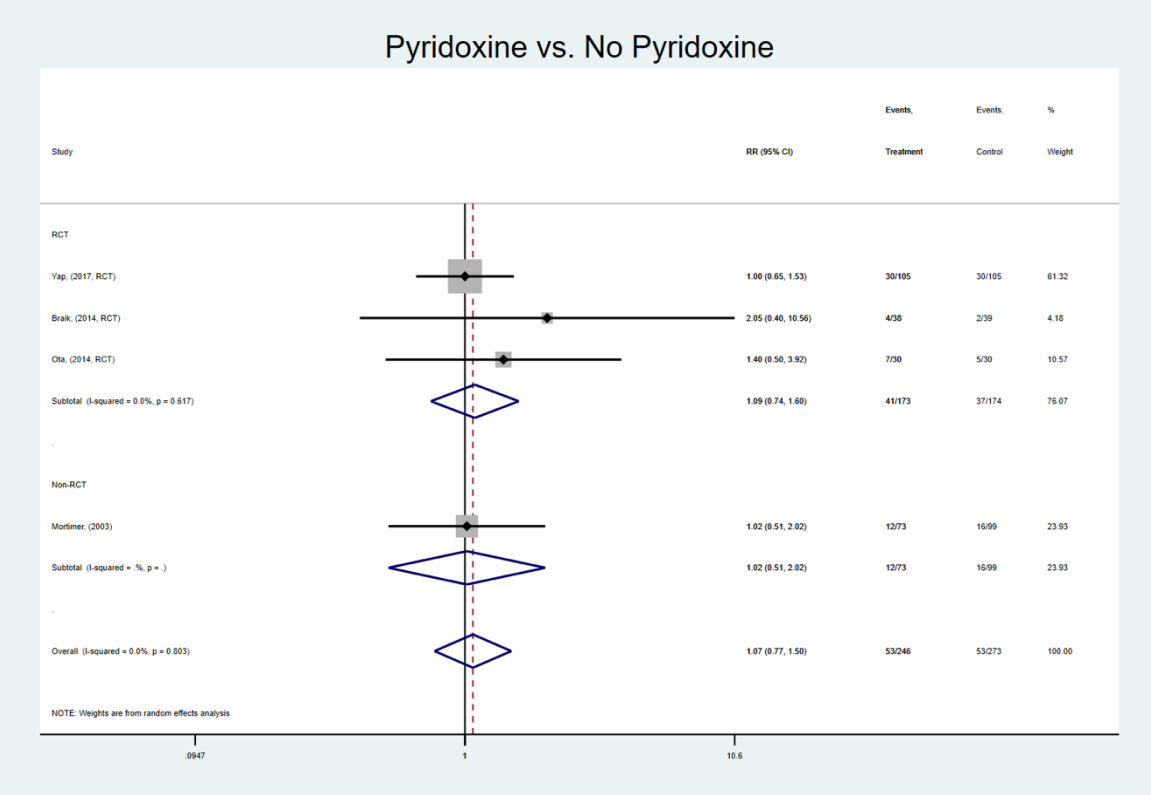

Figure S8. Risk of hand foot syndrome from chemotherapy. Grade 2 (NCI-CTCAE criteria)

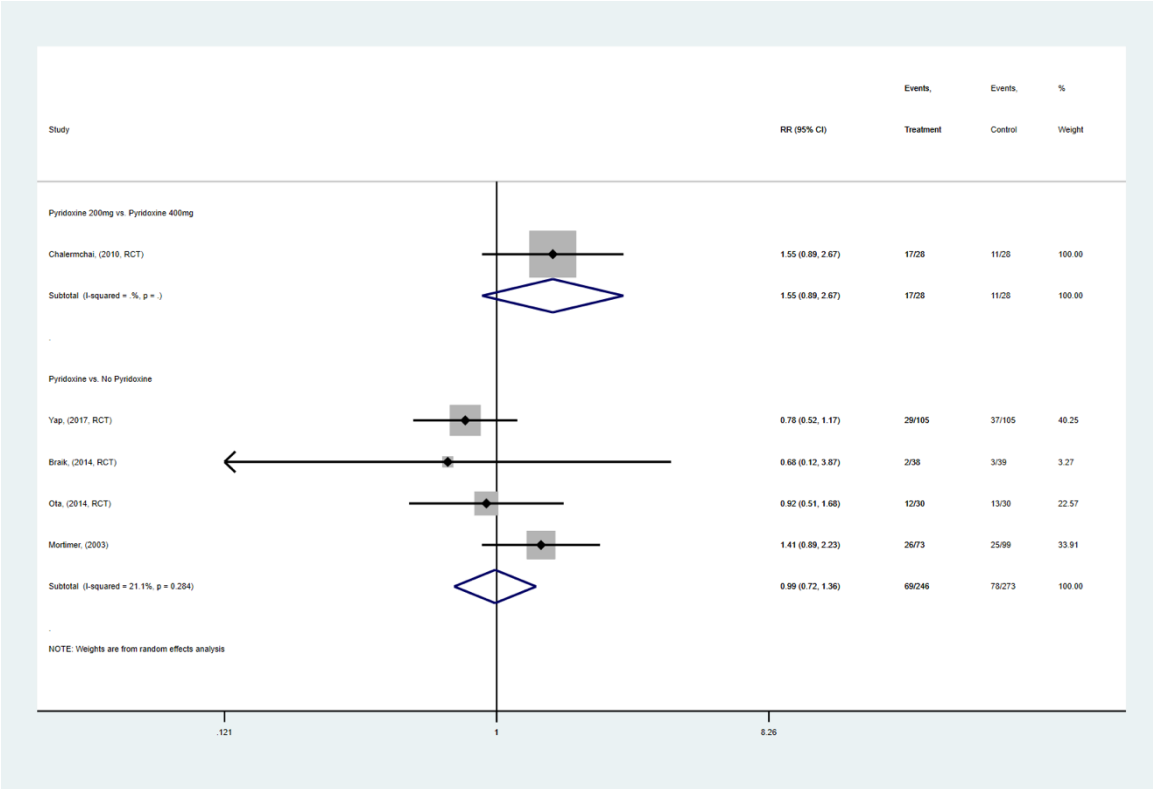

Figure S9. Risk of hand foot syndrome from chemotherapy

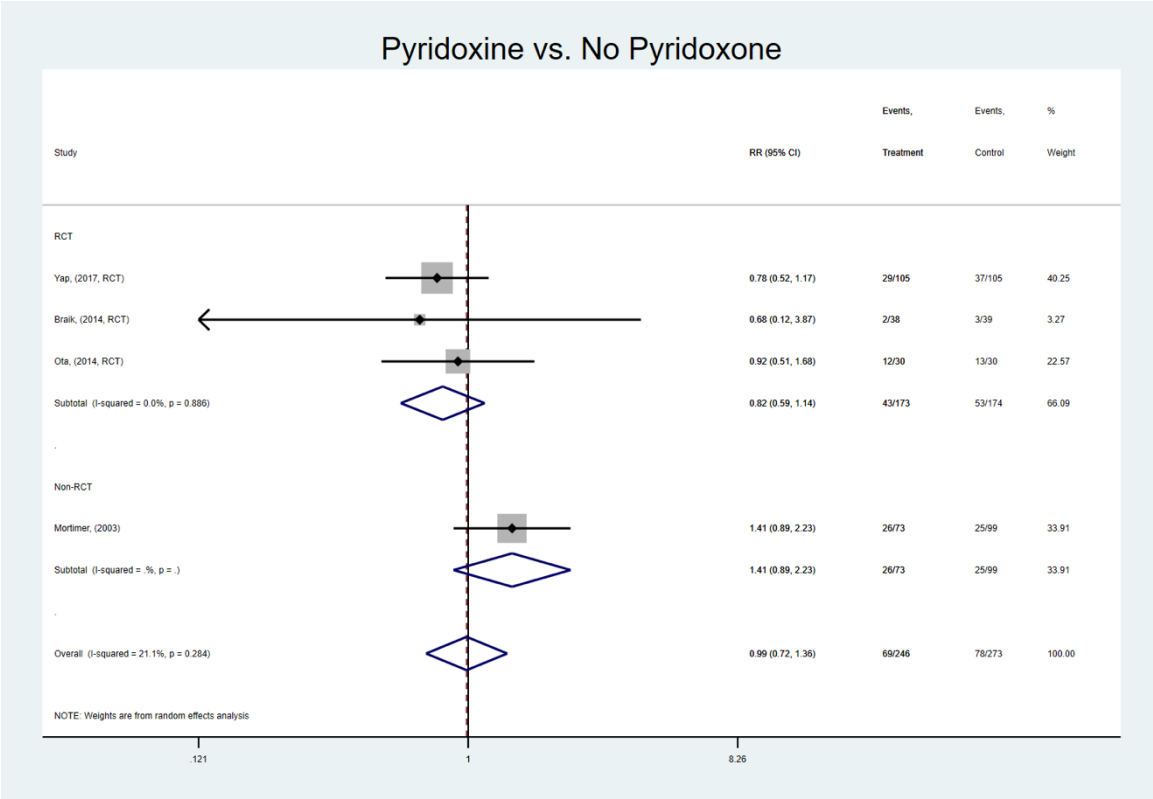

Figure S10. Risk of hand foot syndrome from chemotherapy. Grade 3 (NCI-CTCAE criteria)

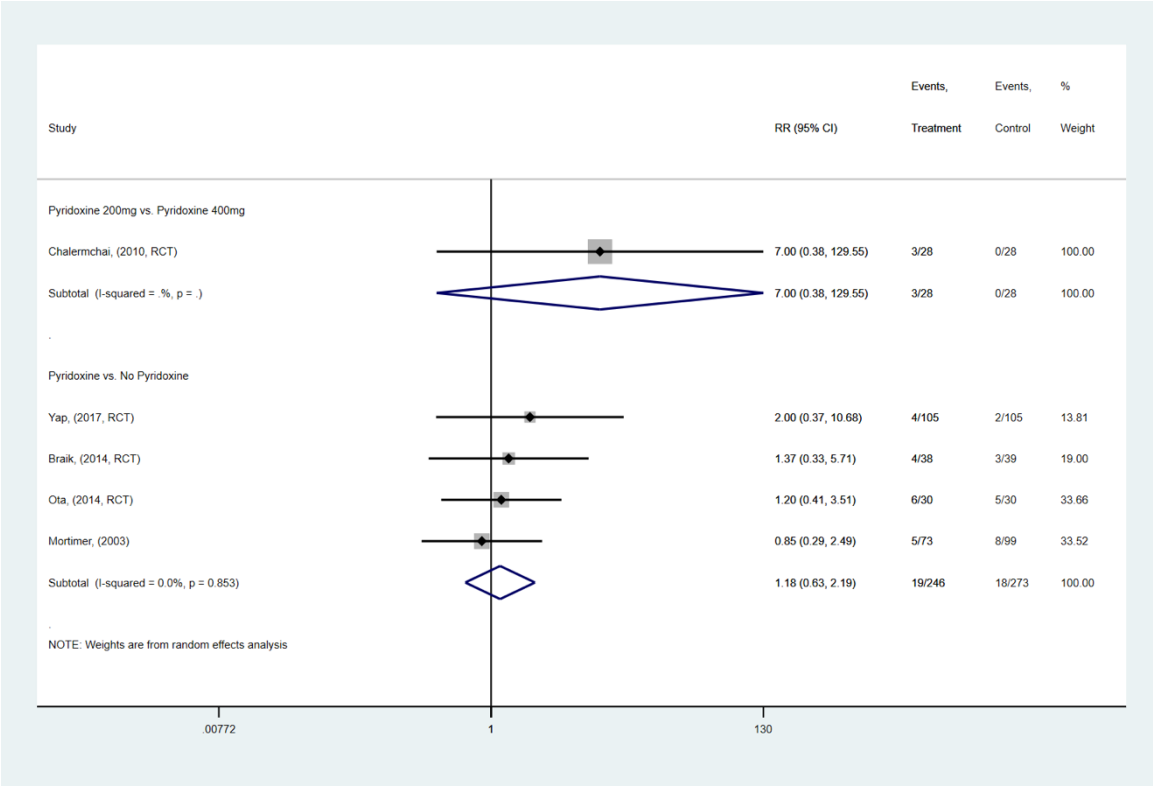

Figure S11. Risk of hand foot syndrome from chemotherapy

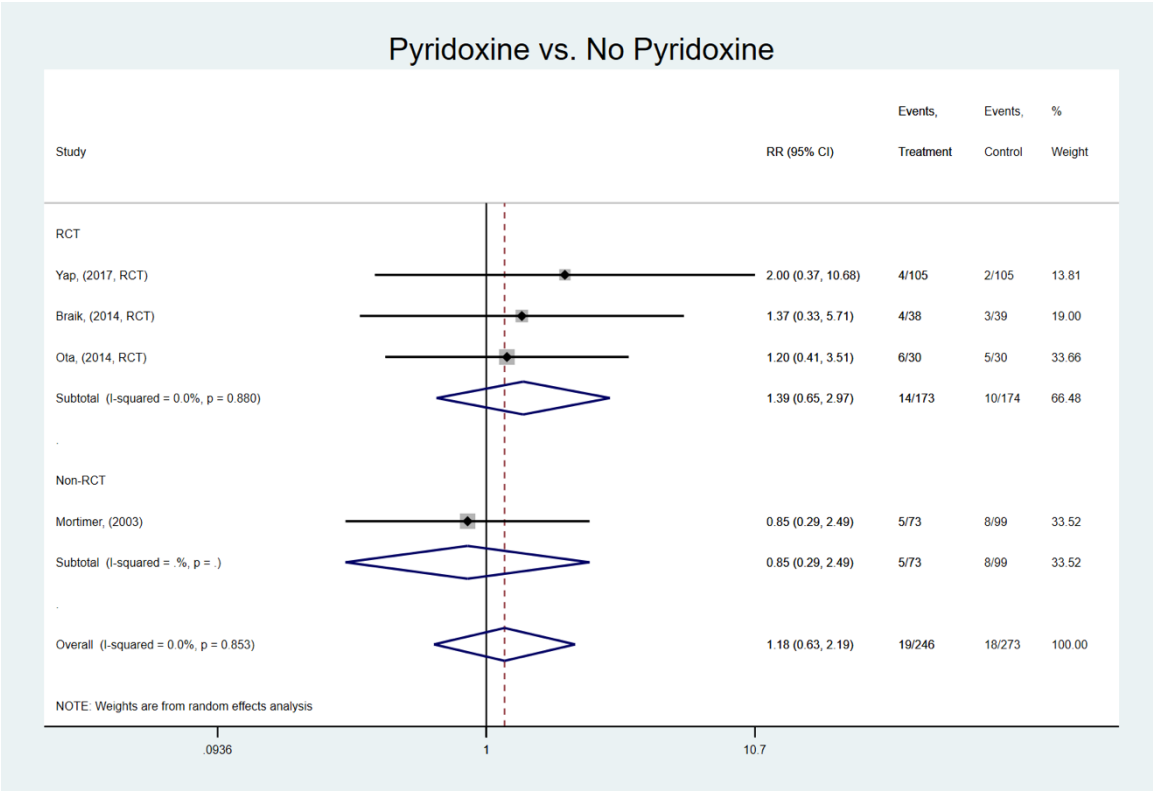

Table 1. Characteristics of studies in the meta-analysis by comparison

A. Characteristics of studies in the meta-analysis reporting the prevention and/or treatment of acneiform rash from cancer treatment with EGFR inhibitors

Study Label (Author, Y)	Design*	Number of Patients (total, arm1/ arm 2)	Age in yr (mean, arm 1/ arm 2)	% Males	BMI (mean, arm 1/ arm 2)	Cancer type	Cancer treatment received	Purpose of intervention (For treatment/ prevention)	First Arm (Intervention)	Second Arm (Control)	Follow up (Months)	Outcomes Reported
Arrieta, 2015	RCT (NCT01880515)	90 (45/45)	56.6/57.5	26.7/26.7	24.75/24.9	Lung cancer [Non-Small Cell Lung Cancer (NSCLC)] Stage IIIB (intervention: 3; control: 5); Stage IV (intervention: 42; control:40)	Afatinib 40 mg/day.	Prevention	Tetracycline	Control	Median, Intervention: 10.7; control: 10.9	1. Risk of rash and alopecia: National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 4.0, grade 1/2/3/4/ ≥2 and all grade 2. Risk of pruritis: National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 4.0, grade 1/2/3/4/ ≥2 and all grade 3. Risk of adverse events from intervention: National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 4.0, Paronychia, Xerosis, Pyogenic granuloma, Foliculitis, photosensitivity, skin fissure, trichomegaly, Hirsutisim, curly hair grade 1/2/3/4/ ≥2 and all grade,

Jatoi, 2008	RCT (N03CB)	61 (31/30)	71/63	48/77	NR	Lung cancer: 31; Gastrointestinal cancer: 16; Other:14.	Epidermal growth factor receptor (EGFR) inhibitors	Prevention	Tetracycline	Placebo	2	1. Risk of rash : National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 3.0 physician-reported and patient-reported, grade 2 or >50% surface area and any grade 2. Quality of life : SKINDEX-16 (a skin-specific quality of life index) questionnaire 3. Risk of adverse events from intervention: CTCAE 3.0, Anorexia grade 2, Constipation grade 2, Dyspepsia grade 2/3, Fatigue grade 2/3, Nausea grade 1/2/3, Abdominal pain grade 1/2/3, Vomiting grade 1/2/3
Jatoi, 2011	RCT (supplementary N03CB)	65 (33/32)	Median 67/61	70/56	NR	Lung cancer intervention: 8; placebo: 8. Gastrointestinal cancer intervention: 19; placebo: 20. Other intervention: 6; placebo: 4.	Epidermal growth factor receptor (EGFR) inhibitors; Gefitinibe:1, Cetuximab: 42, others: 22.	Prevention	Tetracycline	Placebo	longest 2	1. Risk of rash : National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 3.0 physician-reported, grade 2 or >50% surface area and any grade 2. Risk of adverse events from intervention: CTCAE 3.0, Nausea grade 1/2, Vomiting grade 1/2, Diarrhea grade 1/2/3/4, Abdominal pain grade 1/2

Lacouture, 2010	RCT	95 (48/47)	60/61	67/55	NR	Colorectal cancer Metastatic	Panitumumab 6.0 mg/kg every 2 weeks with FOLFIRI chemotherapy and at 9.0 mg/kg every 3 weeks with irinotecan chemotherapy.	Prevention/ treatment	Pre-Emptive skin treatment (Use of skin moisturizers, sunscreen, topical steroid, and doxycycline 100 mg BID)	Reactive skin treatment (any treatments the investigator deemed necessary for the management of emergent skin toxicity and could be administered at any time during weeks 1 to 6)	Pre-emptive skin treatment: 7.5, Reactive skin treatment: 10.18	1. Risk of pustular rash : modified Common Terminology Criteria for Adverse Events version 3.0 2. Risk of Pruritus : modified Common Terminology Criteria for Adverse Events version 3.0 3. Quality of life : DLQI questionnaire

Melosky, 2015	RCT (NCT00473083)	150 (100/50)	Median 64.9	Prophylactic minocycline: 66, Reactive:46/46	NR	Lung cancer [Non-Small Cell Lung Cancer (NSCLC)] Stage IIIb/IV	Erlotinib, 150 mg/day.	Prevention/ treatment	Prophylactic minocycline/ Reactive treatment (Topical clindamycin plus hydrocortisone with or without minocycline at rash occurrence per grade; Scalp lesions were treated with a topical solution containing clindamycin 2% with triamcinolone acetonide 0.1% until resolution)	Control	NR	**Prophylactic minocycline:** 1. Risk of rash: National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 3.0, grade 1/2/3 and all grade 2. Quality of life: total QOL Score (The Dermatology Quality of Life Index was analyzed as the total score) 3. Risk of adverse events from intervention: National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE), Pancreatitis grade 2, Dry skin any grade, Skin pain grade 1, Blister grade 3 and Rash grade 3 **Reactive treatment:** 1. Severity/change in rash: National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 3.0, grade 1/2/3 and all grade 2. Quality of life: total QOL Score 3. Risk of adverse events from intervention: CTCAE, Dry skin grade 1, Skin pain grade 1, Blister any grade and Rash any grade 4. Rate of treatment discontinuation

Shinohara, 2015	Comparative observational study	96 (44/52)	66/67	63.6/55.8	NR	Pancreatic cancer Stage III: 20; Stage IV 76.	Erlotinib plus gemcitabine. Erlotinib was administered at a dose of 100 mg daily, and gemcitabine was administered intravenously over 30 min at a dose of 1,000 mg/m2 once every week for 3 consecutive weeks; each treatment cycle lasted for 4 weeks.	Prevention/ treatment	Prophylactic minocycline	Deferred minocycline	1.5	1. Risk of acneiform rash : National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 4.0 grade 1/≥2 and any grade 2. Risk of adverse events from intervention: CTCAE 4.0, any toxicity from minocycline, Leukocytes, Neutropenia, Hemoglobin, Platelets, Nausea, Vomiting, Diarrhea, Fatigue, Vertigo, interstitial lung disease-like syndrome, AST, ALT, Bilirubin, ALP, Creatinine, grade ≥3 and any grade 3. Time to develop the acneiform rash : median time to first occurrence of acneiform rash of any grade of severity 4. Rate of treatment interruption

Yamada, 2015	Comparative observational study	38 (25/13)	62.5/62.4	64/69	NR	Metastatic colorectal cancer	Panitumumab alone: 12, Panitumumab + mFOLFOX6: 19, Panitumumab + FOLFIRI: 5, Panitumumab + CPT-11: 2.	Prevention	Oral minocycline, standard skin care and reactive topical steroid	No intervention	NR	1. Risk of acneiform rash: Common Terminology Criteria for Adverse Events (CTCAE) v4.0 acneiform rash grade 0/1/2/3/≥2 2. Pruritis : Common Terminology Criteria for Adverse Events (CTCAE) v4.0 Pruritis grade 0/1/2/≥2 3. Risk of adverse events from intervention: Common Terminology Criteria for Adverse Events (CTCAE) v4.0 Dry skin grade 0/1/2/≥2, Paronychia grade 0/1/2/3/≥2, Hypomagnesemia grade 0/1/2/≥2, Oral mucositis grade 0/1/2/3/≥2 and Diarrhea grade 0/1/2/3/≥2

B. Characteristics of studies in the meta-analysis reporting the prevention and/or treatment of hand foot syndrome from chemotherapy

Study Label (Author, Y)	Design*	Number of Patients (total, arm1/ arm 2)	Age in yr (mean, arm 1/ arm 2)	% Males	BMI (mean, arm 1/ arm 2)	Cancer type	Cancer treatment received	Purpose of intervention (For treatment/ prevention)	First Arm (Intervention)	Second Arm (Control)	Follow up (Months)	Outcomes Reported
Braik, 2014	RCT (NCT00767689)	77 (38/39)	53.5/53.5	38	NR	Breast cancer : 27 ; Colorectal cancer : 29 ; Pancreas cancer : 8 ; Stomach cancer : 4 ; Sarcoma : 4 ; Bile duct cancer : 4 ; Unknown primary cancer : 1.	Capecitabine alone (1,000 mg/m2 twice daily on days 1 through 14 in every 21-day cycle): 43; Capecitabine + oxaliplatin: 24; Capecitabine + lapatinib: 5; Capecitabine + trastuzumab: 3; Capecitabine + cetuximab: 2.	Prevention	Pyridoxine	Placebo	6	Risk of Hand Foot Syndrome : National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 3.0 grade 1/2/3/all-grade
Chalermchai, 2010	RCT	56 (28/28)	54.7/58.7	39.3/46.4	NR	Breast cancer: 17; Colorectal cancer: 39;	Capecitabine 2000–2500 mg/m^2 per day for adjuvant or palliative treatment.	Prevention	Pyridoxine 200 mg	Pyridoxine 400 mg	5.5	1. Risk of PPE: Common Toxicity Criteria (CTC) version 3.0 grade 2/3/≥2 2. Time to develop PPE: grade ≥ 2, median (range) 3. Rate of treatment interruption/discontinuation

Corrie, 2012	RCT	106 (53/53)	70/70	37.7/37.7	NR	Breast cancer: 38; Colorectal cancer: 68.	Capecitabine starting dose was planned to be 1250 mg/m^2 administered orally, twice daily, for 2 weeks followed by 7 days rest	Prevention	Pyridoxine	Placebo	3 months after stopping treatment	Risk of Hand Foot Syndrome: National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 3.0 grade 3-4 and all grade
Kang, 2010	RCT	360 (180/180)	56/56	67/58	NR	Colorectal cancer: 215; Stomach cancer:132; Bile duct cancer: 12; Duodenum cancer: 1.	Docetaxel, capecitabine, and cisplatin:30; Capecitabine and cisplatin:90; Capecitabine: 230.	Prevention/ treatment	Pyridoxine	Placebo	NR	1. Risk of Hand Foot Syndrome: National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 2.0 grade 2-3 and all grade 2. Time to develop Hand Foot Syndrome: grade 2-3, median 3. Improvement rate of Hand Foot Syndrome: grade 2-3 4. No change rate of Hand Foot Syndrome: grade 2-3 5. Aggravation rate of Hand Foot Syndrome: grade 2-3

Mortimer, 2003	Comparative observational study	198 (99/99)	59	7	NR	Breast cancer: 156; Colorectal cancer: 42	Capecitabine (the median initial starting dosage was 2024 mg/m^2/day (range 506-3083 mg/m^2), median number of cycles: 5 (2-6), administered for 14 consecutive days on a 21-day cycle.	Prevention/ treatment	Pyridoxine prophylaxis/ treatment	No pyridoxine	NR	1. Risk of Hand Foot Syndrome: Common Toxicity Criteria (CTC) scores for hand and foot skin reactions, grade1/2/3 and all grade 2. Improvement rate of Hand Foot Syndrome: defined as patient self-report of symptom improvement (i.e., reduction in CTC score), grade1/2/3 and all grade
Ota, 2014	RCT	60 (30/30)	65.2/62.8	43/40	NR	Colorectal cancer Stage IIIA: 11; Stage IIIB: 30; Stage IIIC: 19.	Eight 3-week cycles of 2,500 mg/m2 of capecitabine per day in two divided doses for 14 days, followed by a 7-day rest period.	Prevention	Concomitant pyridoxine	No pyridoxine	NR	1. Risk of Hand Foot Syndrome: National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 3.0 grade 0/1/2/3/≥2 2. Time to develop Hand Foot Syndrome: all grade and grade > 2, median
Yap, 2017	RCT (NCT00486213)	210 (105/105)	58/57	23/23	NR	Breast cancer: 138; colorectal cancer: 60; Other: 12.	Capecitabine at a dose of at least 1000mg/m2 twice daily for the first 2 weeks (rounded up or down to the closest dose comprising 150 mg and 500 mg tablets) on a 3-weekly cycle.	Prevention	Pyridoxine	Placebo	NR	1. Risk of Hand Foot Syndrome: National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 Hand Foot Syndrome grade 0/1/2/3/≥2 2. Quality of life (functional limitations): EuroQol EQ-5D-3L questionnaire-Mobility/ Self care/ Usual activities

C. Characteristics of studies in the meta-analysis reporting the prevention and/or treatment of hand foot skin reaction from multikinase inhibitors

Study Label (Author, Y)	Design *	Number of Patients (total, arm1/ arm 2)	Age in yr (mean, arm 1/ arm 2)	% Males	BMI (mean, arm 1/ arm 2)	Cancer type	Cancer treatment received	Purpose of intervention (For treatment/ prevention)	First Arm (Intervention)	Second Arm (Control)	Follow up (Months)	Outcomes Reported
Lin, 2017	RCT (NCT01 098760)	63 (29/34)	62	NR	NR	Hepatocellular carcinoma Stage II: 8; IIIA:32; IIIB:17; IIIC:13; IV: 81.	Sorafenib 400 mg (2 X 200-mg tablets) twice daily (BID) on a continuous schedule.	Prevention	Corticosteroid ointment	Non-corticosteroid ointment	6	1. Risk of HFSR: HFSR grade 3 and 3-5 in 3 and 6 weeks 2. HFSR score overall and in 3, 6 weeks 3. Time to develop HFSR: median (range)
Ren, 2015	RCT (NCT01 934829	871 (439/432)	Median 51.8/52.0	85.9/ 85.2	NR	Hepatocellular carcinoma Advanced	Sorafenib 400 mg twice per day.	Prevention	Urea based cream + Best supportive care	Best supportive care	3.5	1. Risk of HFSR: grade 1/2/3/≥2 and any grade 2. Quality of life (functional limitations): HFSR-associated HRQL (The HF-QoL questionnaire) 3. Time to develop HFSR: median (range) 4. HFSR symptom and daily activity score in week 2-14
Shinohara, 2013	RCT (UMIN0 000020 16)	33 (17/16)	65/68	82/75	24/24	Renal cell carcinoma	Sorafenib (400 mg b.i.d.).	Treatment	Hydrocolloid dressing containing ceramide with a low-friction external surface	10% urea cream	NR	1. Risk of HFSR: NCI-CTCAE version 4.0 HFSR on the soles grade 1/2/3 and on the palms grade 0/1/2/3 2. Time to develop HFSR: grade 2 or 3, median (range) 3. Risk of adverse events from intervention: mild skin sore

D. Characteristics of studies in the meta-analysis reporting the prevention and/or treatment of chemotherapy-induced alopecia

Study Label (Author, Y)	Design*	Number of Patients (total, arm1/ arm 2)	Age in yr (mean, arm 1/ arm 2)	% Males	BMI (mean, arm 1/ arm 2)	Cancer type	Cancer treatment received	Purpose of intervention (For treatment/ prevention)	First Arm (Intervention)	Second Arm (Control)	Follow up (Months)	Outcomes Reported
Kargar, 2011	Quasi-experimental	63 (31/32)	35	36.5	NR	NR	Taxol, ABVD, and BEP; Cyclophosphamide, Adriamycin and Vincristine plus Prednisolone (CHOP)	Prevention	Scalp-cooling	Non-scalp-cooling	NR	Risk of alopecia: World Health Organization (WHO) criteria for alopecia grade 0,1 and 2,3
van den Hurk, 2013	Comparative observational study	246 (160/86)	52/51	4	NR	Breast cancer: 229; Ovarian cancer: 8; Lung cancer: 4; GI cancer: 3; Prostate cancer: 2.	FEC (5-fluorouracil + epirubicin + cyclophosphamide): 140; Paclitaxel combination: 11; Docetaxel (mono/combination): 9; ACTH (adriamycin + cyclophosphamide + paclitaxel + herceptin): 22; FAC (5-fluorouracil + adriamycin + cyclophosphamide): 16; FECD (5-fluorouracil + epirubicin + cyclophosphamide + docetaxel): 13; DAC (docetaxel + adriamycin + cyclophosphamide): 19; Other: 9.	Prevention	Scalp-cooling	Non-scalp-cooling	NR	1. Risk of alopecia: WHO alopecia grade 0/1/2/3 2. Quality of life: by VAS (Visual Analogue Scale) score

van den Hurk, 2014 (Acta Oncologica)	Comparative observational study (the same study as van den Hurk, 2013)	246 (160/86)	52/51	4	NR	Breast cancer: 229; Ovarian cancer: 8; Lung cancer: 4; GI cancer: 3; Prostate cancer: 2.	FEC (5-fluorouracil + epirubicin + cyclophosphamide): 140; Paclitaxel combination: 11; Docetaxel (mono/combination): 9; ACTH (adriamycin + cyclophosphamide + paclitaxel + herceptin): 22; FAC (5-fluorouracil + adriamycin + cyclophosphamide): 16; FECD (5-fluorouracil + epirubicin + cyclophosphamide + docetaxel): 13; DAC (docetaxel + adriamycin + cyclophosphamide): 19; Other: 9.	Prevention	Scalp-cooling	Non-scalp-cooling	12	1. Quality of life: during chemotherapy, 3 weeks – 6 months after chemotherapy and 6 – 12 months after chemotherapy by SF 6D and VAS score 2. Cost: total patient and total scalp cooling hospital

Search strategy

Q1

Ovid

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials February 2019, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to March 27, 2019, Embase 1974 to 2019 March 29, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to March 29, 2019
Search Strategy:

#	Searches	Results
1	exp epidermal growth factor receptor kinase inhibitor/	109434
2	(afatinib or canertinib or dacomitinib or depatuxizumab or "depatuxizumab mafodotin" or "EGF receptor inhibitor*" or "EGFR inhibitor*" or "epidermal growth factor receptor inhibitor*" or "epidermal growth factor receptor kinase inhibitor*" or "epidermal growth factor receptor protein tyrosine kinase inhibitor*" or "epidermal growth factor receptor tyrosine kinase inhibitor*" or erlotinib or gefitinib or genistein or icotinib or lapatinib or losatuxizumab or mavelertinib or modotuximab or naquotinib or nazartinib or neratinib or olmutinib or osimertinib or pelitinib or poziotinib or "protein tyrosine kinase inhibitor*" or rociletinib or rogaratinib or sapitinib or tarloxotinib or timigutuzumab or tomuzotuximab or trastuzumab or "trastuzumab deruxtecan" or "trastuzumab duocarmazine" or varlitinib).ti,ab,hw,kw.	160263
3	1 or 2	177886
4	exp Acneiform Eruptions/	43778
5	(acne or acneiform or Chloracne or Folliculitis or "PAPA syndrome" or Rash or rashes or "SAPHO syndrome").ti,ab,hw,kw.	209980
6	4 or 5	209980
7	3 and 6	11352
8	exp Antibiotic Prophylaxis/	43047

9	exp Anti-Bacterial Agents/	3884159
10	exp antibiotic agent/	1290716
11	(antibacterial* or "anti-bacterial*" or antibiotic* or "anti-biotic*" or antimicrobial* or "anti-microbial*" or antimycobacterial* or "anti-mycobacterial*" or bacteriocid*).ti,ab,hw,kw.	1513828
12	8 or 9 or 10 or 11	4321407
13	exp Administration, Oral/	544868
14	exp oral drug administration/	544868
15	(oral or orally or "po administration" or "po dosage" or "po dose" or "po drug" or "per os drug" or "per os administration" or "per os dosage" or "per os dose").mp.	2357882
16	13 or 14 or 15	2361254
17	12 and 16	473211
18	(doxycycline or minicycline or minocycline or tetracycline*).ti,ab,hw,kw.	210802
19	17 or 18	649415
20	exp topical treatment/	10277
21	exp Administration, Topical/	199590
22	("topic application*" or "topic medication*" or "topic therap*" or "topic treatment*" or topical*).ti,ab,hw,kw.	327425
23	20 or 21 or 22	399289
24	exp Isotretinoin/	15704
25	isotretinoin.ti,ab,hw,kw.	17101

26	24 or 25	17101
27	23 and 26	2774
28	exp Adrenal Cortex Hormones/	1271905
29	exp corticosteroid/	863222
30	exp corticosteroid therapy/	43632
31	("adrenal cortex hormone*" or "adrenal cortex steroid*" or "adrenal cortical hormone*" or "adrenal cortical steroid*" or "adrenal steroid*" or "adreno cortical steroid*" or "adreno corticosteroid*" or "adrenocortical hormone*" or "adrenocortical steroid*" or adrenocorticosteroid* or adreson or alclometasone or aldosterone or algestone or "algestone acetonide" or amcinonide or amelometasone or beclometasone or budesonide or butixocort or chloroprednisone or ciclesonide or ciprocinonide or clioquinol or clobetasol or clobetasone or clocortolone or cloprednol or "cortical steroid*" or corticalsteroid* or "cortico steroid*" or corticoid* or corticosteroid* or corticosterone or corticotherap* or cortifair or cortisol or cortisone or cortivazol or cortril or deflazacort or dehydrocorticosterone or dehydrocortisone or deoxycorticosterone or dermocorticosteroid* or dexamethasone or diflorasone or diflucortolone or difluprednate or domoprednate or drocinonide or dutimelan or epicortisol or "etiprednol dicloacetate" or fluclorolone or fludrocortisone or fludroxycortide or flumetasone or flumoxonide or flunisolide or fluocinolone or fluocinonide or fluocortin or fluocortolone or fluorometholone or fluprednidene or fluprednisolone or fluticasone or formocortal or "formoterol fumarate" or Glucocorticoid* or glucocorticoidsteroid* or glucocorticosteroid* or glucocortoid* or glycocorticoid* or glycocorticosteroid* or halcinonide or halometasone or halopredone or hydrocortisone or "hydroxy norcorticosterone" or hydroxycorticoid* or hydroxycorticosteroid* or hydroxycorticosterone or hydroxydeoxycorticosterone or hydroxyhydrocortisone or "icometasone enbutate" or isoflupredone or itrocinonide or "locicortolone dicibate" or "lorinden a" or "lorinden t" or loteprednol or mazipredone or medrysone or meprednisone or mineralcorticosteroid* or mineralocorticosteroid* or minerocorticoid* or "mometasone furoate" or nicocortonide or nivacortol or nordeoxycorticosterone or oropivalone or oxohydrocortisone or oxycorticosteroid* or paramethasone or prednisolone or prednisone or pregnenolone or procinonide or promestriene or resocortol or rimexolone or rofleponide or steroid* or tetrahydrodeoxycorticosterone or ticabesone or timobesone or tipredane or tixocortol or triamcinolone or "ulobetasol propionate" or uniderm or zoticasone).ti,ab,hw,kw.	2013926
32	28 or 29 or 30 or 31	2079057

33 (16 or 23) and 32	366980
34 19 or 27 or 33	913650
35 7 and 34	2026
36 exp evidence based medicine/	1145422
37 exp meta analysis/	258169
38 exp Meta-Analysis as Topic/	57039
39 exp "systematic review"/	301029
40 exp Guideline/ or exp Practice Guideline/	522025
41 exp controlled study/	6680981
42 exp Randomized Controlled Trial/	1020185
43 exp triple blind procedure/	204
44 exp Double-Blind Method/	439387
45 exp Single-Blind Method/	79905
46 exp latin square design/	361
47 exp Placebos/	388945
48 exp Placebo Effect/	11206
49 exp comparative study/	3128292
50 exp intervention studies/	39732

51	exp Cross-Sectional Studies/	586142
52	exp Cross-Over Studies/	138371
53	exp Cohort Studies/	2429563
54	exp longitudinal study/	377741
55	exp retrospective study/	1496634
56	exp prospective study/	1090455
57	exp clinical trial/	2198408
58	clinical study/	156767
59	exp case-control studies/	1149203
60	exp confidence interval/	164691
61	exp multivariate analysis/	514350
62	((evidence adj based) or (meta adj analys*) or (systematic* adj3 review*) or guideline* or (control* adj3 study) or (control* adj3 trial) or (randomized adj3 study) or (randomized adj3 trial) or (randomised adj3 study) or (randomised adj3 trial) or "pragmatic clinical trial" or (doubl* adj blind*) or (doubl* adj mask*) or (singl* adj blind*) or (singl* adj mask*) or (tripl* adj blind*) or (tripl* adj mask*) or (trebl* adj blind*) or (trebl* adj mask*) or "latin square" or placebo* or nocebo* or multivariate or "comparative study" or "comparative survey" or "comparative analysis" or (intervention* adj2 study) or (intervention* adj2 trial) or "cross-sectional study" or "cross-sectional analysis" or "cross-sectional survey" or "cross-sectional design" or "prevalence study" or "prevalence analysis" or "prevalence survey" or "disease frequency study" or "disease frequency analysis" or "disease frequency survey" or crossover or "cross-over" or cohort* or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "longitudinal evaluation" or longitudinal* or ((retrospective or "ex post facto") adj3 (study or survey or analysis or design)) or retrospectiv* or "prospective study" or "prospective survey" or "prospective analysis" or prospectiv* or "concurrent study" or "concurrent survey" or "concurrent analysis" or "clinical study" or "clinical trial" or "case control study" or "case base study" or "case referrent study" or "case referent study" or "case referent study" or "case compeer study" or "case comparison study" or "matched case control" or "multicenter study" or "multi-center study" or "odds ratio" or "confidence interval" or "change analysis" or	21782897

	((study or trial or random* or control*) and compar*)).mp,pt.	
63	or/36-62	22337008
64	35 and 63	1539
65	("case study" or "case series" or "clinical series" or "case studies" or (case adj3 report)).mp,pt.	3146591
66	64 not 65	1493
67	limit 66 to (editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in CCTR,CDSR,Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	22
68	66 not 67	1471
69	remove duplicates from 68	1420

Scopus

1	TITLE-ABS-KEY(afatinib or canertinib or dacomitinib or depatuxizumab or "depatuxizumab mafodotin" or "EGF receptor inhibitor*" or "EGFR inhibitor*" or "epidermal growth factor receptor inhibitor*" or "epidermal growth factor receptor kinase inhibitor*" or "epidermal growth factor receptor protein tyrosine kinase inhibitor*" or "epidermal growth factor receptor tyrosine kinase inhibitor*" or erlotinib or gefitinib or genistein or icotinib or lapatinib or losatuxizumab or mavelertinib or modotuximab or naquotinib or nazartinib or neratinib or olmutinib or osimertinib or pelitinib or poziotinib or "protein tyrosine kinase inhibitor*" or rociletinib or rogaratinib or sapitinib or tarloxotinib or timigutuzumab or tomuzotuximab or trastuzumab or "trastuzumab deruxtecan" or "trastuzumab duocarmazine" or varlitinib)
2	TITLE-ABS-KEY(acne or acneiform or Chloracne or Folliculitis or "PAPA syndrome" or Rash or rashes or "SAPHO syndrome")
3	1 and 2
4	TITLE-ABS-KEY(oral or orally or "po administration" or "po dosage" or "po dose" or "po drug" or "per os drug" or "per os administration" or "per os dosage" or "per os dose")
5	TITLE-ABS-KEY("topic application*" or "topic medication*" or "topic therap*" or "topic treatment*" or topical*)
6	TITLE-ABS-KEY(antibacterial* or "anti-bacterial*" or antibiotic* or "anti-biotic*" or antimicrobial* or "anti-microbial*" or antimycobacterial* or "anti-mycobacterial*" or bacteriocid*)
7	TITLE-ABS-KEY(doxycycline or minicycline or minocycline or tetracycline*)
8	TITLE-ABS-KEY(isotretinoin)
9	TITLE-ABS-KEY("adrenal cortex hormone*" or "adrenal cortex steroid*" or "adrenal cortical hormone*" or "adrenal cortical steroid*" or "adrenal steroid*" or "adreno cortical steroid*" or "adreno corticosteroid*" or "adrenocortical hormone*" or "adrenocortical steroid*" or adrenocorticosteroid* or adreson or alclometasone or aldosterone or algestone or "algestone acetonide" or amcinonide or amelometasone or beclometasone or budesonide or butixocort or chloroprednisone or ciclesonide or ciprocinonide or clioquinol or clobetasol or clobetasone or clocortolone or cloprednol or "cortical steroid*" or corticalsteroid* or "cortico steroid*" or corticoid* or corticosteroid* or corticosterone or corticotherap* or cortifair or cortisol or cortisone or cortivazol or cortril or deflazacort or dehydrocorticosterone or dehydrocortisone or deoxycorticosterone or dermocorticosteroid* or dexamethasone or diflorasone or diflucortolone or difluprednate or domoprednate or drocinonide or dutimelan or epicortisol or "etiprednol dicloacetate" or fluclorolone or fludrocortisone or fludroxycortide or flumetasone or flumoxonide or flunisolide or fluocinolone or fluocinonide or fluocortin or fluocortolone or fluorometholone or fluprednidene or fluprednisolone or fluticasone or formocortal or "formoterol fumarate" or Glucocorticoid* or glucocorticoidsteroid* or glucocorticosteroid* or glucocortoid* or glycocorticoid* or glycocorticosteroid* or halcinonide or halometasone or halopredone or hydrocortisone or "hydroxy norcorticosterone" or hydroxycorticoid* or hydroxycorticosteroid* or hydroxycorticosterone or hydroxydeoxycorticosterone or hydroxyhydrocortisone or "icometasone enbutate" or isoflupredone or itrocinonide or "locicortolone dicibate" or "lorinden a" or "lorinden t" or loteprednol or mazipredone or medrysone or meprednisone or mineralcorticosteroid* or mineralocorticosteroid* or minerocorticoid* or "mometasone furoate" or nicocortonide or nivacortol or nordeoxycorticosterone or oropivalone or oxohydrocortisone or oxycorticosteroid* or paramethasone or prednisolone or prednisone or pregnenolone or procinonide or promestriene or resocortol or rimexolone or rofleponide or steroid* or tetrahydrodeoxycorticosterone or ticabesone or timobesone or tipredane or tixocortol or triamcinolone or "ulobetasol propionate" or uniderm or zoticasone)
10	(4 and 6) or 7 or (5 and 8) or (4 and 9) or (5 and 9)

11	TITLE-ABS-KEY((evidence W/1 based) or (meta W/1 analys*) or (systematic* W/3 review*) or guideline* or (control* W/3 study) or (control* W/3 trial) or (randomized W/3 study) or (randomized W/3 trial) or (randomised W/3 study) or (randomised W/3 trial) or "pragmatic clinical trial" or (doubl* W/1 blind*) or (doubl* W/1 mask*) or (singl* W/1 blind*) or (singl* W/1 mask*) or (tripl* W/1 blind*) or (tripl* W/1 mask*) or (trebl* W/1 blind*) or (trebl* W/1 mask*) or "latin square" or placebo* or nocebo* or multivariate or "comparative study" or "comparative survey" or "comparative analysis" or (intervention* W/2 study) or (intervention* W/2 trial) or "cross-sectional study" or "cross-sectional analysis" or "cross-sectional survey" or "cross-sectional design" or "prevalence study" or "prevalence analysis" or "prevalence survey" or "disease frequency study" or "disease frequency analysis" or "disease frequency survey" or crossover or "cross-over" or cohort* or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "longitudinal evaluation" or longitudinal* or ((retrospective or "ex post facto") W/3 (study or survey or analysis or design)) or retrospectiv* or "prospective study" or "prospective survey" or "prospective analysis" or prospectiv* or "concurrent study" or "concurrent survey" or "concurrent analysis" or "clinical study" or "clinical trial" or "case control study" or "case base study" or "case referrent study" or "case referent study" or "case referent study" or "case compeer study" or "case comparison study" or "matched case control" or "multicenter study" or "multi-center study" or "odds ratio" or "confidence interval" or "change analysis" or ((study or trial or random* or control*) and compar*))
12	3 and 10 and 11
13	TITLE-ABS-KEY("case study" OR "case series" OR "clinical series" OR "case studies" OR (case W/3 report))
14	12 and not 13
15	DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
16	14 and not 15
17	INDEX(embase) OR INDEX(medline) OR PMID(0* OR 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*)
18	16 and not 17

Q2

Ovid

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials February 2019, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to March 27, 2019, Embase 1974 to 2019 March 29, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to March 29, 2019
Search Strategy:

#	Searches	Results
1	exp Antineoplastic Agents/	3134201
2	chemotherapy/	171593
3	Drug Therapy/	634713
4	("Antineoplastic Agent*" or chemotherap* or "drug therap*").ti,ab,hw,kw.	2623645
5	1 or 2 or 3 or 4	4503323
6	infus*.ti,ab,hw,kw.	767170
7	5 and 6	164187
8	exp taxane derivative/ or exp cyclophosphamide plus doxorubicin plus taxane/	12765
9	exp fluorouracil/	179919
10	exp doxorubicin/ or exp doxorubicin derivative/	235347
11	exp cytarabine derivative/ or exp cytarabine/	73284
12	exp capecitabine/	30136
13	(5FU or capecitabine or cytarabine or doxorubicin or fluorouracil or Taxane).ti,ab,hw,kw.	501581

14	or/7-13	631082
15	exp Hand-Foot Syndrome/	11229
16	("acral erythema*" or "foot hand dermal reaction*" or "foot hand skin reaction*" or "foot hand syndrome*" or "hand foot dermal reaction*" or "hand foot skin reaction*" or "hand foot syndrome*" or "palmar plantar erythrodysaesthesia*" or "palmar plantar erythrodysesthesia*" or "palmoplantar erythrodysaesthesia*" or "palmoplantar erythrodysesthesia*").ti,ab,hw,kw.	15907
17	15 or 16	15907
18	14 and 17	9138
19	exp Hypothermia, Induced/	34006
20	exp cooling/	17588
21	(((induced or therap*) adj3 hypothermia*) or cold or cooling or "targeted temperature*").ti,ab,hw,kw.	404091
22	exp Emollients/	10934
23	(Emollient* or lotion*).ti,ab,hw,kw.	16616
24	exp pyridoxine/ or exp pyridoxine derivative/	35939
25	(Pyridoxine or "vitamin B 6" or "vitamin B6").ti,ab,hw,kw.	41435
26	exp topical treatment/	10277
27	exp Administration, Topical/	199590
28	("topic application*" or "topic medication*" or "topic therap*" or "topic treatment*" or topical*).ti,ab,hw,kw.	327425
29	exp Adrenal Cortex Hormones/	1271905
30	exp corticosteroid/	863222

31	exp corticosteroid therapy/	43632
32	("adrenal cortex hormone*" or "adrenal cortex steroid*" or "adrenal cortical hormone*" or "adrenal cortical steroid*" or "adrenal steroid*" or "adreno cortical steroid*" or "adreno corticosteroid*" or "adrenocortical hormone*" or "adrenocortical steroid*" or adrenocorticosteroid* or adreson or alclometasone or aldosterone or algestone or "algestone acetonide" or amcinonide or amelometasone or beclometasone or budesonide or butixocort or chloroprednisone or ciclesonide or ciprocinonide or clioquinol or clobetasol or clobetasone or clocortolone or cloprednol or "cortical steroid*" or corticalsteroid* or "cortico steroid*" or corticoid* or corticosteroid* or corticosterone or corticotherap* or cortifair or cortisol or cortisone or cortivazol or cortril or deflazacort or dehydrocorticosterone or dehydrocortisone or deoxycorticosterone or dermocorticosteroid* or dexamethasone or diflorasone or diflucortolone or difluprednate or domoprednate or drocinonide or dutimelan or epicortisol or "etiprednol dicloacetate" or fluclorolone or fludrocortisone or fludroxycortide or flumetasone or flumoxonide or flunisolide or fluocinolone or fluocinonide or fluocortin or fluocortolone or fluorometholone or fluprednidene or fluprednisolone or fluticasone or formocortal or "formoterol fumarate" or Glucocorticoid* or glucocorticoidsteroid* or glucocorticosteroid* or glucocortoid* or glycocorticoid* or glycocorticosteroid* or halcinonide or halometasone or halopredone or hydrocortisone or "hydroxy norcorticosterone" or hydroxycorticoid* or hydroxycorticosteroid* or hydroxycorticosterone or hydroxydeoxycorticosterone or hydroxyhydrocortisone or "icometasone enbutate" or isoflupredone or itrocinonide or "locicortolone dicibate" or "lorinden a" or "lorinden t" or loteprednol or mazipredone or medrysone or meprednisone or mineralcorticosteroid* or mineralocorticosteroid* or minerocorticoid* or "mometasone furoate" or nicocortonide or nivacortol or nordeoxycorticosterone or oropivalone or oxohydrocortisone or oxycorticosteroid* or paramethasone or prednisolone or prednisone or pregnenolone or procinonide or promestriene or resocortol or rimexolone or rofleponide or steroid* or tetrahydrodeoxycorticosterone or ticabesone or timobesone or tipredane or tixocortol or triamcinolone or "ulobetasol propionate" or uniderm or zoticasone).ti,ab,hw,kw.	2013926
33	29 or 30 or 31 or 32	2079057
34	(26 or 27 or 28) and 33	83875
35	or/19-25	470180
36	34 or 35	550091
37	18 and 36	406

38	exp protein tyrosine kinase inhibitor/	257093
39	exp B Raf kinase/	25873
40	exp sorafenib/	30165
41	exp sunitinib/	23900
42	exp cabozantinib/	2622
43	exp regorafenib/	2793
44	exp axitinib/	4538
45	exp pazopanib/	6759
46	exp vandetanib/	4234
47	exp vemurafenib/	7623
48	exp dabrafenib/	3301
49	(axitinib or "B Raf kinase" or "B Raf protein*" or BRAF or cabozantinib or dabrafenib or "multikinase inhibitor*" or pazopanib or "protein B Raf" or "proto oncogene proteins B raf" or regorafenib or sorafenib or sunitinib or TKI or "tyrosine kinase inhibitor*" or "tyrosine protein kinase inhibitor*" or vandetanib or vemurafenib).ti,ab,hw,kw.	175716
50	or/38-49	340489
51	exp urea/ or exp urea derivative/	224306
52	exp clobetasol/	4142
53	(clobetasol or urea).ti,ab,hw,kw.	255434
54	34 or 51 or 52 or 53	442972

55 50 and 54	14821
56 55 and prevent*.ti,ab,hw,kw.	856
57 37 or 56	1251
58 exp evidence based medicine/	1145422
59 exp meta analysis/	258169
60 exp Meta-Analysis as Topic/	57039
61 exp "systematic review"/	301029
62 exp Guideline/ or exp Practice Guideline/	522025
63 exp controlled study/	6680981
64 exp Randomized Controlled Trial/	1020185
65 exp triple blind procedure/	204
66 exp Double-Blind Method/	439387
67 exp Single-Blind Method/	79905
68 exp latin square design/	361
69 exp Placebos/	388945
70 exp Placebo Effect/	11206
71 exp comparative study/	3128292
72 exp intervention studies/	39732

73	exp Cross-Sectional Studies/	586142
74	exp Cross-Over Studies/	138371
75	exp Cohort Studies/	2429563
76	exp longitudinal study/	377741
77	exp retrospective study/	1496634
78	exp prospective study/	1090455
79	exp clinical trial/	2198408
80	clinical study/	156767
81	exp case-control studies/	1149203
82	exp confidence interval/	164691
83	exp multivariate analysis/	514350
84	((evidence adj based) or (meta adj analys*) or (systematic* adj3 review*) or guideline* or (control* adj3 study) or (control* adj3 trial) or (randomized adj3 study) or (randomized adj3 trial) or (randomised adj3 study) or (randomised adj3 trial) or "pragmatic clinical trial" or (doubl* adj blind*) or (doubl* adj mask*) or (singl* adj blind*) or (singl* adj mask*) or (tripl* adj blind*) or (tripl* adj mask*) or (trebl* adj blind*) or (trebl* adj mask*) or "latin square" or placebo* or nocebo* or multivariate or "comparative study" or "comparative survey" or "comparative analysis" or (intervention* adj2 study) or (intervention* adj2 trial) or "cross-sectional study" or "cross-sectional analysis" or "cross-sectional survey" or "cross-sectional design" or "prevalence study" or "prevalence analysis" or "prevalence survey" or "disease frequency study" or "disease frequency analysis" or "disease frequency survey" or crossover or "cross-over" or cohort* or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "longitudinal evaluation" or longitudinal* or ((retrospective or "ex post facto") adj3 (study or survey or analysis or design)) or retrospectiv* or "prospective study" or "prospective survey" or "prospective analysis" or prospectiv* or "concurrent study" or "concurrent survey" or "concurrent analysis" or "clinical study" or "clinical trial" or "case control study" or "case base study" or "case referrent study" or "case referent study" or "case referent study" or "case compeer study" or "case comparison study" or "matched case control" or "multicenter study" or "multi-center study" or "odds ratio" or "confidence interval" or "change analysis" or	21790891

	((study or trial or random* or control*) and compar*) or ((prevention or preventive) adj3 (trial or study or analysis or survey))).mp,pt.	
85	or/58-84	22344740
86	57 and 85	792
87	("case study" or "case series" or "clinical series" or "case studies" or (case adj3 report)).mp,pt.	3146591
88	86 not 87	772
89	limit 88 to (editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in CCTR,CDSR,Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	5
90	88 not 89	767
91	remove duplicates from 90	697

Scopus

1	TITLE-ABS-KEY(("Antineoplastic Agent*" or chemotherap* or "drug therap*") and infus*)
2	TITLE-ABS-KEY(5FU or capecitabine or cytarabine or doxorubicin or fluorouracil or Taxane)
3	TITLE-ABS-KEY("acral erythema*" OR "foot hand dermal reaction*" OR "foot hand skin reaction*" OR "foot hand syndrome*" OR "hand foot dermal reaction*" OR "hand foot skin reaction*" OR "hand foot syndrome*" OR "palmar plantar erythrodysaesthesia*" OR "palmar plantar erythrodysesthesia*" OR "palmoplantar erythrodysaesthesia*" OR "palmoplantar erythrodysesthesia*")
4	(1 or 2) and 3
5	TITLE-ABS-KEY(((induced or therap*) W/3 hypothermia*) or cold or cooling or "targeted temperature*")
6	TITLE-ABS-KEY(Emollient* or lotion*)
7	TITLE-ABS-KEY(Pyridoxine or "vitamin B 6" or "vitamin B6")
8	TITLE-ABS-KEY(("topic application*" or "topic medication*" or "topic therap*" or "topic treatment*" or topical*) and ("adrenal cortex hormone*" or "adrenal cortex steroid*" or "adrenal cortical hormone*" or "adrenal cortical steroid*" or "adrenal steroid*" or "adreno cortical steroid*" or "adreno corticosteroid*" or "adrenocortical hormone*" or "adrenocortical steroid*" or adrenocorticosteroid* or adreson or alclometasone or aldosterone or algestone or "algestone acetonide" or amcinonide or amelometasone or beclometasone or budesonide or butixocort or chloroprednisone or ciclesonide or ciprocinonide or clioquinol or clobetasol or clobetasone or clocortolone or cloprednol or "cortical steroid*" or corticalsteroid* or "cortico steroid*" or corticoid* or corticosteroid* or corticosterone or corticotherap* or cortifair or cortisol or cortisone or cortivazol or cortril or deflazacort or dehydrocorticosterone or dehydrocortisone or deoxycorticosterone or dermocorticosteroid* or dexamethasone or diflorasone or diflucortolone or difluprednate or domoprednate or drocinonide or dutimelan or epicortisol or "etiprednol dicloacetate" or fluclorolone or fludrocortisone or fludroxycortide or flumetasone or flumoxonide or flunisolide or fluocinolone or fluocinonide or fluocortin or fluocortolone or fluorometholone or fluprednidene or fluprednisolone or fluticasone or formocortal or "formoterol fumarate" or Glucocorticoid* or glucocorticoidsteroid* or glucocorticosteroid* or glucocortoid* or glycocorticoid* or glycocorticosteroid* or halcinonide or halometasone or halopredone or hydrocortisone or "hydroxy norcorticosterone" or hydroxycorticoid* or hydroxycorticosteroid* or hydroxycorticosterone or hydroxydeoxycorticosterone or hydroxyhydrocortisone or "icometasone enbutate" or isoflupredone or itrocinonide or "locicortolone dicibate" or "lorinden a" or "lorinden t" or loteprednol or mazipredone or medrysone or meprednisone or mineralcorticosteroid* or mineralocorticosteroid* or minerocorticoid* or "mometasone furoate" or nicocortonide or nivacortol or nordeoxycorticosterone or oropivalone or oxohydrocortisone or oxycorticosteroid* or paramethasone or prednisolone or prednisone or pregnenolone or procinonide or promestriene or resocortol or rimexolone or rofleponide or steroid* or tetrahydrodeoxycorticosterone or ticabesone or timobesone or tipredane or tixocortol or triamcinolone or "ulobetasol propionate" or uniderm or zoticasone))
9	4 and (5 or 6 or 7 or 8)
10	TITLE-ABS-KEY(axitinib or "B Raf kinase" or "B Raf protein*" or BRAF or cabozantinib or dabrafenib or "multikinase inhibitor*" or pazopanib or "protein B Raf" or "proto oncogene proteins B raf" or regorafenib or sorafenib or sunitinib or TKI or "tyrosine kinase inhibitor*" or "tyrosine protein kinase inhibitor*" or vandetanib or vemurafenib)
11	TITLE-ABS-KEY(clobetasol or urea)
12	TITLE-ABS-KEY(prevent*)
13	10 and (8 or 11) and 12

14	9 or 13
15	TITLE-ABS-KEY((evidence W/1 based) or (meta W/1 analys*) or (systematic* W/3 review*) or guideline* or (control* W/3 study) or (control* W/3 trial) or (randomized W/3 study) or (randomized W/3 trial) or (randomised W/3 study) or (randomised W/3 trial) or "pragmatic clinical trial" or (doubl* W/1 blind*) or (doubl* W/1 mask*) or (singl* W/1 blind*) or (singl* W/1 mask*) or (tripl* W/1 blind*) or (tripl* W/1 mask*) or (trebl* W/1 blind*) or (trebl* W/1 mask*) or "latin square" or placebo* or nocebo* or multivariate or "comparative study" or "comparative survey" or "comparative analysis" or (intervention* W/2 study) or (intervention* W/2 trial) or "cross-sectional study" or "cross-sectional analysis" or "cross-sectional survey" or "cross-sectional design" or "prevalence study" or "prevalence analysis" or "prevalence survey" or "disease frequency study" or "disease frequency analysis" or "disease frequency survey" or crossover or "cross-over" or cohort* or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "longitudinal evaluation" or longitudinal* or ((retrospective or "ex post facto") W/3 (study or survey or analysis or design)) or retrospectiv* or "prospective study" or "prospective survey" or "prospective analysis" or prospectiv* or "concurrent study" or "concurrent survey" or "concurrent analysis" or "clinical study" or "clinical trial" or "case control study" or "case base study" or "case referrent study" or "case referent study" or "case referent study" or "case compeer study" or "case comparison study" or "matched case control" or "multicenter study" or "multi-center study" or "odds ratio" or "confidence interval" or "change analysis" or ((study or trial or random* or control*) and compar*) or ((prevention or preventive) W/3 (trial or study or analysis or survey)))
16	14 and 15
17	TITLE-ABS-KEY("case study" OR "case series" OR "clinical series" OR "case studies" OR (case W/3 report))
18	16 and not 17
19	DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
20	18 and not 19
21	INDEX(embase) OR INDEX(medline) OR PMID(0* OR 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*)
22	20 and not 21

Q3

Ovid

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials February 2019, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to March 27, 2019, Embase 1974 to 2019 March 29, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to March 29, 2019
Search Strategy:

#	Searches	Results
1	exp Immunotherapy/	458099
2	exp immunological antineoplastic agent/	216351
3	pembrolizumab/	8882
4	nivolumab/	12190
5	atezolizumab/	2767
6	durvalumab/	2005
7	avelumab/	1199
8	Ipilimumab/	12163
9	((("biologic response modifier" or "biological response modifier" or BRM or immune or immunoglobulin or immunological or targeted) adj3 (therap* or treatment* or intervention* or management or drug* or agent* or inhibitor*)) or atezolizumab or avelumab or durvalumab or immunotherap* or Ipilimumab or nivolumab or "PD1 inhibitor*" or "PD-1 inhibitor*" or "PD-L1 inhibitor*" or pembrolizumab).ti,ab,hw,kw.	609451
10	or/1-9	1015023
11	exp Pruritus/	98781

12	(itch or itching or pruritis or pruritus).ti,ab,hw,kw.	132344
13	11 or 12	137636
14	10 and 13	9057
15	exp topical treatment/	10277
16	exp Administration, Topical/	199590
17	("topic application*" or "topic medication*" or "topic therap*" or "topic treatment*" or topical*).ti,ab,hw,kw.	327425
18	exp Adrenal Cortex Hormones/	1271905
19	exp corticosteroid/	863222
20	exp corticosteroid therapy/	43632
21	("adrenal cortex hormone*" or "adrenal cortex steroid*" or "adrenal cortical hormone*" or "adrenal cortical steroid*" or "adrenal steroid*" or "adreno cortical steroid*" or "adreno corticosteroid*" or "adrenocortical hormone*" or "adrenocortical steroid*" or adrenocorticosteroid* or adreson or alclometasone or aldosterone or algestone or "algestone acetonide" or amcinonide or amelometasone or beclometasone or budesonide or butixocort or chloroprednisone or ciclesonide or ciprocinonide or clioquinol or clobetasol or clobetasone or clocortolone or cloprednol or "cortical steroid*" or corticalsteroid* or "cortico steroid*" or corticoid* or corticosteroid* or corticosterone or corticotherap* or cortifair or cortisol or cortisone or cortivazol or cortril or deflazacort or dehydrocorticosterone or dehydrocortisone or deoxycorticosterone or dermocorticosteroid* or dexamethasone or diflorasone or diflucortolone or difluprednate or domoprednate or drocinonide or dutimelan or epicortisol or "etiprednol dicloacetate" or fluclorolone or fludrocortisone or fludroxycortide or flumetasone or flumoxonide or flunisolide or fluocinolone or fluocinonide or fluocortin or fluocortolone or fluorometholone or fluprednidene or fluprednisolone or fluticasone or formocortal or "formoterol fumarate" or Glucocorticoid* or glucocorticoidsteroid* or glucocorticosteroid* or glucocortoid* or glycocorticoid* or glycocorticosteroid* or halcinonide or halometasone or halopredone or hydrocortisone or "hydroxy norcorticosterone" or hydroxycorticoid* or hydroxycorticosteroid* or hydroxycorticosterone or hydroxydeoxycorticosterone or hydroxyhydrocortisone or "icometasone enbutate" or isoflupredone or itrocinonide or "locicortolone dicibate" or "lorinden a" or "lorinden t" or loteprednol or mazipredone or medrysone or meprednisone or mineralcorticosteroid* or mineralocorticosteroid* or minerocorticoid* or "mometasone furoate" or nicocortonide or	2013926

nivacortol or nordeoxycorticosterone or oropivalone or oxohydrocortisone or oxycorticosteroid* or paramethasone or prednisolone or prednisone or pregnenolone or procinonide or promestriene or resocortol or rimexolone or rofleponide or steroid* or tetrahydrodeoxycorticosterone or ticabesone or timobesone or tipredane or tixocortol or triamcinolone or "ulobetasol propionate" or uniderm or zoticasone).ti,ab,hw,kw.	
22 18 or 19 or 20 or 21	2079057
23 (15 or 16 or 17) and 22	83875
24 exp Emollients/	10934
25 (Emollient* or lotion*).ti,ab,hw,kw.	16616
26 24 or 25	19961
27 14 and (23 or 26)	520
28 exp evidence based medicine/	1145422
29 exp meta analysis/	258169
30 exp Meta-Analysis as Topic/	57039
31 exp "systematic review"/	301029
32 exp Guideline/ or exp Practice Guideline/	522025
33 exp controlled study/	6680981
34 exp Randomized Controlled Trial/	1020185
35 exp triple blind procedure/	204
36 exp Double-Blind Method/	439387
37 exp Single-Blind Method/	79905

38	exp latin square design/	361
39	exp Placebos/	388945
40	exp Placebo Effect/	11206
41	exp comparative study/	3128292
42	exp intervention studies/	39732
43	exp Cross-Sectional Studies/	586142
44	exp Cross-Over Studies/	138371
45	exp Cohort Studies/	2429563
46	exp longitudinal study/	377741
47	exp retrospective study/	1496634
48	exp prospective study/	1090455
49	exp clinical trial/	2198408
50	clinical study/	156767
51	exp case-control studies/	1149203
52	exp confidence interval/	164691
53	exp multivariate analysis/	514350
54	((evidence adj based) or (meta adj analys*) or (systematic* adj3 review*) or guideline* or (control* adj3 study) or (control* adj3 trial) or (randomized adj3 study) or (randomized adj3 trial) or (randomised adj3 study) or (randomised adj3 trial) or "pragmatic clinical trial" or (doubl* adj blind*) or (doubl* adj mask*) or (singl* adj blind*) or (singl* adj mask*) or (tripl* adj blind*) or (tripl* adj mask*) or (trebl* adj blind*) or (trebl* adj mask*) or "latin square" or placebo* or nocebo* or multivariate or "comparative study" or "comparative survey" or "comparative analysis" or (intervention* adj2	21790891

	study) or (intervention* adj2 trial) or "cross-sectional study" or "cross-sectional analysis" or "cross-sectional survey" or "cross-sectional design" or "prevalence study" or "prevalence analysis" or "prevalence survey" or "disease frequency study" or "disease frequency analysis" or "disease frequency survey" or crossover or "cross-over" or cohort* or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "longitudinal evaluation" or longitudinal* or ((retrospective or "ex post facto") adj3 (study or survey or analysis or design)) or retrospectiv* or "prospective study" or "prospective survey" or "prospective analysis" or prospectiv* or "concurrent study" or "concurrent survey" or "concurrent analysis" or "clinical study" or "clinical trial" or "case control study" or "case base study" or "case referrent study" or "case referent study" or "case referent study" or "case compeer study" or "case comparison study" or "matched case control" or "multicenter study" or "multi-center study" or "odds ratio" or "confidence interval" or "change analysis" or ((study or trial or random* or control*) and compar*) or ((prevention or preventive) adj3 (trial or study or analysis or survey))).mp,pt.	
55	or/28-54	22344740
56	27 and 55	302
57	("case study" or "case series" or "clinical series" or "case studies" or (case adj3 report)).mp,pt.	3146591
58	56 not 57	262
59	limit 58 to (editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in CCTR,CDSR,Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	3
60	58 not 59	259
61	remove duplicates from 60	233

Scopus

1 TITLE-ABS-KEY((("biologic response modifier" or "biological response modifier" or BRM or immune or immunoglobulin or immunological or targeted) W/3 (therap* or treatment* or intervention* or management or drug* or agent* or inhibitor*)) OR atezolizumab OR avelumab OR durvalumab OR immunotherap* OR Ipilimumab OR nivolumab OR "PD1 inhibitor*" OR "PD-1 inhibitor*" OR "PD-L1 inhibitor*" OR pembrolizumab)

2 TITLE-ABS-KEY(itch OR itching OR pruritis OR pruritus)

3 TITLE-ABS-KEY(("topic application*" or "topic medication*" or "topic therap*" or "topic treatment*" or topical*) and ("adrenal cortex hormone*" or "adrenal cortex steroid*" or "adrenal cortical hormone*" or "adrenal cortical steroid*" or "adrenal steroid*" or "adreno cortical steroid*" or "adreno corticosteroid*" or "adrenocortical hormone*" or "adrenocortical steroid*" or adrenocorticosteroid* or adreson or alclometasone or aldosterone or algestone or "algestone acetonide" or amcinonide or amelometasone or beclometasone or budesonide or butixocort or chloroprednisone or ciclesonide or ciprocinonide or clioquinol or clobetasol or clobetasone or clocortolone or cloprednol or "cortical steroid*" or corticalsteroid* or "cortico steroid*" or corticoid* or corticosteroid* or corticosterone or corticotherap* or cortifair or cortisol or cortisone or cortivazol or cortril or deflazacort or dehydrocorticosterone or dehydrocortisone or deoxycorticosterone or dermocorticosteroid* or dexamethasone or diflorasone or diflucortolone or difluprednate or domoprednate or drocinonide or dutimelan or epicortisol or "etiprednol dicloacetate" or fluclorolone or fludrocortisone or fludroxycortide or flumetasone or flumoxonide or flunisolide or fluocinolone or fluocinonide or fluocortin or fluocortolone or fluorometholone or fluprednidene or fluprednisolone or fluticasone or formocortal or "formoterol fumarate" or Glucocorticoid* or glucocorticoidsteroid* or glucocorticosteroid* or glucocortoid* or glycocorticoid* or glycocorticosteroid* or halcinonide or halometasone or halopredone or hydrocortisone or "hydroxy norcorticosterone" or hydroxycorticoid* or hydroxycorticosteroid* or hydroxycorticosterone or hydroxydeoxycorticosterone or hydroxyhydrocortisone or "icometasone enbutate" or isoflupredone or itrocinonide or "locicortolone dicibate" or "lorinden a" or "lorinden t" or loteprednol or mazipredone or medrysone or meprednisone or mineralcorticosteroid* or mineralocorticosteroid* or minerocorticoid* or "mometasone furoate" or nicocortonide or nivacortol or nordeoxycorticosterone or oropivalone or oxohydrocortisone or oxycorticosteroid* or paramethasone or prednisolone or prednisone or pregnenolone or procinonide or promestriene or resocortol or rimexolone or rofleponide or steroid* or tetrahydrodeoxycorticosterone or ticabesone or timobesone or tipredane or tixocortol or triamcinolone or "ulobetasol propionate" or uniderm or zoticasone))

4 TITLE-ABS-KEY(Emollient* or lotion*)

5 TITLE-ABS-KEY((evidence W/1 based) or (meta W/1 analys*) or (systematic* W/3 review*) or guideline* or (control* W/3 study) or (control* W/3 trial) or (randomized W/3 study) or (randomized W/3 trial) or (randomised W/3 study) or (randomised W/3 trial) or "pragmatic clinical trial" or (doubl* W/1 blind*) or (doubl* W/1 mask*) or (singl* W/1 blind*) or (singl* W/1 mask*) or (tripl* W/1 blind*) or (tripl* W/1 mask*) or (trebl* W/1 blind*) or (trebl* W/1 mask*) or "latin square" or placebo* or nocebo* or multivariate or "comparative study" or "comparative survey" or "comparative analysis" or (intervention* W/2 study) or (intervention* W/2 trial) or "cross-sectional study" or "cross-sectional analysis" or "cross-sectional survey" or "cross-sectional design" or "prevalence study" or "prevalence analysis" or "prevalence survey" or "disease frequency study" or "disease frequency analysis" or "disease frequency survey" or crossover or "cross-over" or cohort* or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "longitudinal evaluation" or longitudinal* or ((retrospective or "ex post facto") W/3 (study or survey or analysis or design)) or retrospectiv* or "prospective study" or "prospective survey" or "prospective analysis" or prospectiv* or "concurrent study" or

	"concurrent survey" or "concurrent analysis" or "clinical study" or "clinical trial" or "case control study" or "case base study" or "case referrent study" or "case referent study" or "case referent study" or "case compeer study" or "case comparison study" or "matched case control" or "multicenter study" or "multi-center study" or "odds ratio" or "confidence interval" or "change analysis" or ((study or trial or random* or control*) and compar*) or ((prevention or preventive) W/3 (trial or study or analysis or survey)))
6	1 and 2 and (3 or 4) and 5
7	TITLE-ABS-KEY("case study" OR "case series" OR "clinical series" OR "case studies" OR (case W/3 report))
8	6 and not 7
9	DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
10	8 and not 9
11	INDEX(embase) OR INDEX(medline) OR PMID(0* OR 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*)
12	10 and not 11

Q4

Ovid

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials February 2019, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to March 27, 2019, Embase 1974 to 2019 March 29, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to March 29, 2019
Search Strategy:

#	Searches	Results
1	exp Cytotoxins/	169158
2	exp cytotoxic agent/	47638
3	(cytolysin* or cytotoxic* or cytotoxin* or Granzymes or haematoxin* or "Haemolysin Protein*" or haemolytic* or haemotoxin* or hematoxin* or "Hemolysin Protein*" or hemolytic* or hemotoxin* or Leukocidins or Perforin or Zinostatin).ti,ab,hw,kw.	948518
4	1 or 2 or 3	1072533
5	exp Alopecia/	59433
6	(Alopecia* or atrichosis or baldness or "Cronkhite Canada syndrome*" or "follicular mucinoses" or "follicular mucinosis" or "hair loss" or "hair losses" or hairlessness or "loose anagen hair syndrome*" or "loose anagen syndrome*" or "mucinosis follicularis" or pseudopelade).ti,ab,hw,kw.	85624
7	5 or 6	85655
8	4 and 7	4241
9	exp Hypothermia, Induced/	34006
10	exp cooling/	17588
11	(((induced or therap*) adj3 hypothermia*) or cold or cooling or "targeted temperature*").ti,ab,hw,kw.	404091

12	9 or 10 or 11	404120
13	exp minoxidil/	9082
14	(minoxidil or rogaine).ti,ab,hw,kw.	10029
15	13 or 14	10029
16	8 and (12 or 15)	166
17	limit 16 to (editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in CCTR,CDSR,Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	1
18	16 not 17	165
19	remove duplicates from 18	146

Scopus

1	TITLE-ABS-KEY(cytolysin* OR cytotoxic* OR cytotoxin* OR Granzymes OR haematoxin* OR "Haemolysin Protein*" OR haemolytic* OR haemotoxin* OR hematoxin* OR "Hemolysin Protein*" OR hemolytic* OR hemotoxin* OR Leukocidins OR Perforin OR Zinostatin)
2	TITLE-ABS-KEY(Alopecia* OR atrichosis OR baldness OR "Cronkhite Canada syndrome*" OR "follicular mucinoses" OR "follicular mucinosis" OR "hair loss" OR "hair losses" OR hairlessness OR "loose anagen hair syndrome*" OR "loose anagen syndrome*" OR "mucinosis follicularis" OR pseudopelade)
3	1 and 2
4	TITLE-ABS-KEY(((induced or therap*) W/3 hypothermia*) or cold or cooling or "targeted temperature*")
5	TITLE-ABS-KEY(minoxidil OR rogaine)
6	3 and (4 or 5)
7	DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
8	6 and not 7
9	INDEX(embase) OR INDEX(medline) OR PMID(0* OR 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*)
10	8 and not 9