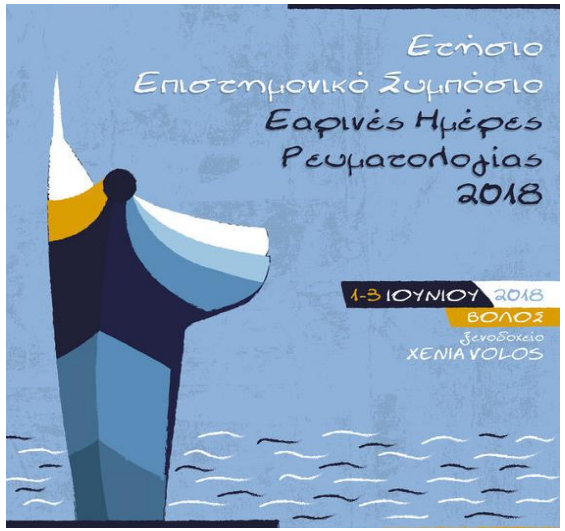
ΝΕΕΣ ΔΙΕΘΝΕΙΣ ΣΥΣΤΑΣΕΙΣ (2017-2018)

Συστάσεις (ACR) για την περιεγχειρητική χρήση των αντιρευματικών φαρμάκων

Θεμιστοκλής Ι.Τεμεκονίδης

Ρευματολόγος -Καβάλα



Σύγκρουση συμφερόντων

Καμμία!

Συστάσεις ACR (2008)

Table 3. Recommendations for withholding biologic disease-modifying antirheumatic drugs in preoperative and perioperative periods*

Therapeutic agent	Withhold medication for ≥1 week before/ after surgery
Abatacept†	X
Anti–tumor necrosis factor α†	X
Rituximab†	X

* Therapies are listed alphabetically. X = contraindication.
† When considering discontinuation, the pharmacokinetics of the drugs and the infectious risk of the surgery being performed should be considered.

Συστάσεις ACR 2008 για “non biologics”

- Καμμία σύσταση, λόγω ελλείψεως evidence!

Συστάσεις ACR (2017)

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SPECIAL ARTICLE

2017 American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty

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DMARDs: CONTINUE these medications through surgery.	**Dosing Interval**	**Continue/Withhold**
Methotrexate	Weekly	Continue
Sulfasalazine	Once or twice daily	Continue
Hydroxychloroquine	Once or twice daily	Continue
Leflunomide (Arava)	Daily	Continue
Doxycycline	Daily	Continue

BIOLOGIC AGENTS: STOP these medications prior to surgery and schedule surgery at the end of the dosing cycle. RESUME medications at minimum 14 days after surgery in the absence of wound healing problems, surgical site infection, or systemic infection.	**Dosing Interval**	**Schedule Surgery (relative to last biologic agent dose administered) during**
Adalimumab (Humira) /Biosimilar	Weekly or every 2 weeks	Week 2 or 3
Etanercept (Enbrel) /Biosimilar	Weekly or twice weekly	Week 2
Golimumab (Simponi)	Every 4 weeks (SQ) or every 8 weeks (IV)	Week 5 Week 9
Infliximab (Remicade) /Biosimilar	Every 4, 6, or 8 weeks	Week 5, 7, or 9
Abatacept (Orencia)	Monthly (IV) or weekly (SQ)	Week 5 Week 2
Certolizumab (Cimzia)	Every 2 or 4 weeks	Week 3 or 5
Rituximab (Rituxan)	2 doses 2 weeks apart every 4-6 months	Month 7
Tocilizumab (Actemra)	Every week (SQ) or every 4 weeks (IV)	Week 2 Week 5
Anakinra (Kineret)	Daily	Day 2
Secukinumab (Cosentyx)	Every 4 weeks	Week 5
Ustekinumab (Stelara)	Every 12 weeks	Week 13
Belimumab (Benlysta)	Every 4 weeks	Week 5
Tofacitinib (Xeljanz): STOP this medication 7 days prior to surgery.	Daily or twice daily	7 days after last dose

SEVERE SLE-SPECIFIC MEDICATIONS: CONTINUE these medications in the perioperative period.	**Dosing Interval**	**Continue/Withhold**
Mycophenolate mofetil	Twice daily	Continue
Azathioprine	Daily or twice daily	Continue
Cyclosporine	Twice daily	Continue
Tacrolimus	Twice daily (IV and PO)	Continue
NOT-SEVERE SLE: DISCONTINUE these medications 1 week prior to surgery	**Dosing Interval**	**Continue/Withhold**
Mycophenolate mofetil	Twice daily	Withhold
Azathioprine	Daily or twice daily	Withhold
Cyclosporine	Twice daily	Withhold
Tacrolimus	Twice daily (IV and PO)	Withhold

Recommendation/strength of recommendation (bold indicates conditional)	Level of evidence
RA, SpA including AS and PsA, JIA, or SLE: Continue the current dose of methotrexate, leflunomide, hydroxychloroquine, and/or sulfasalazine (nonbiologic DMARDs) for patients undergoing elective THA or TKA. • RCTs of continuing vs. discontinuing DMARDs at the time of surgery revealed that the risk of infections was not increased, but in fact decreased, when DMARDs were continued, with an RR of 0.39 (95% CI 0.17–0.91) (37,38). Evidence indicates a low infection risk with these DMARDs in settings other than THA and TKA (37). • Disease flares after surgery occur frequently, and continuing DMARDs decreases the risk (RR 0.06 [95% CI 0.0–1.10]) (37,40), yet flares were significantly less important than infection for the Patient Panel.	Low to moderate
RA, SpA including AS and PsA, JIA, or SLE: Withhold all current biologic agents (see Figure 1) prior to surgery in patients undergoing elective THA or TKA, and plan the surgery at the end of the dosing cycle for that specific medication. • RCTs (nonsurgical) demonstrated an increase in infection risk associated with use of all biologic agents (41–87). • Avoiding infection was significantly more important to patients than flares for patients with RA and JIA. • Meta-analysis and network meta-analysis revealed that infection risk for biologic agents is strongly associated with high-dose therapy and may not be associated with low-dose biologic agents (42). • Serum half-life may not correspond to the duration of the immunosuppressant effect, so the dosing cycle was chosen as more relevant in determining the withholding interval (88–91). • Until further studies have clarified and established differences in risk between biologic agents, there was insufficient evidence to support separating biologic agent management in the perioperative period (43–89). • For SLE, there was a paucity of data supporting perioperative benefit in SLE (93–95). • A systematic review of rituximab vs. placebo (and occasionally vs. control treatment including nonbiologic DMARDs) in nonsurgical patients with RA and SLE revealed the risk of all serious adverse events with a range of RRs from 0.85 (95% CI 0.62–1.17) to 0.89 (95% CI 0.7–1.14) (59,92). • Observational studies reveal that patients with SLE, particularly those with active or severe SLE, are at a higher risk for adverse events after surgery. • Belimumab is indicated for use in not-severe SLE, which is not thought to increase perioperative risk (95,96). • As an example, using this guideline, patients treated with rituximab every 6 months would schedule their surgery, when possible, at the week after the first withheld dose during month 7. Patients receiving belimumab, which is given every 4 weeks, would schedule their surgery during week 5. • Patients treated with adalimumab, dosed at 2-week intervals, would plan their surgery in week 3, while patients treated with infliximab, when dosed every 8 weeks, would schedule their surgery in the week after the first withheld dose during week 9.	Low
RA, SpA including AS and PsA, or JIA: Withhold tofacitinib for at least 7 days prior to surgery in patients undergoing THA or TKA. • Indirect evidence from systematic reviews and meta-analyses of tofacitinib vs. placebo (and occasionally vs. control treatment including nonbiologic DMARDs) in nonsurgical patients shows that the risk of serious infections was increased with tofacitinib with an incidence rate of 2.91 (95% CI 2.27–3.74) (97) and higher risk of all infections with an RR of 5.7 (95% CI 1.8–18.1) (48). • Although this drug has an extremely short serum half-life, little is known about the duration of immunosuppression after the drug is withheld. Therefore, the Panel recognized that the recommendation for the duration of withholding may change in the future, as physician and patient experience with this drug grows (41,47,48,51,77,79,97,98).	Low
Severe SLE: Continue the current dose of mycophenolate mofetil, azathioprine, cyclosporine, or tacrolimus through the surgical period in all patients undergoing THA or TKA (see Figure 1). • The Panel recognized that there is a great deal of uncertainty and little published experience regarding risks associated with perioperative medication management in patients with severe SLE. • Indirect evidence with organ transplant patients supports continuing anti-rejection therapy without interruption at the time of surgery (99,100). • Decisions regarding elective surgery in patients with severe SLE should be made on an individual basis with the patient's rheumatologist.	Low
SLE (not severe): Withhold the current dose of mycophenolate mofetil, azathioprine, cyclosporine, or tacrolimus 1 week prior to surgery in all patients undergoing THA or TKA. • The time course to flares in not-severe SLE is not known. • The morbidity of prosthetic joint infection may be more severe than a flare in SLE that is not severe. • These medications can be withheld 1 week prior to surgery, permitting return of some immune function, and restarted at 3–5 days after surgery in the absence of wound healing complications or infection at the surgical site or elsewhere. • There are multiple mechanisms postulated for immunosuppression with these medications, including leukopenia, interference with T cell costimulatory signaling, and blocking the de novo pathway of purine synthesis, with different time courses for onset and reversal (101,102). • Suggest a conservative withhold of 7 days prior to surgery until additional research increases understanding of these medications.	Low

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Recommendation/strength of recommendation (bold indicates conditional)	Level of evidence
SLE (not severe): Withhold the current dose of mycophenolate mofetil, azathioprine, cyclosporine, or tacrolimus 1 week prior to surgery in all patients undergoing THA or TKA. • The time course to flares in not-severe SLE is not known. • The morbidity of prosthetic joint infection may be more severe than a flare in SLE that is not severe. • These medications can be withheld 1 week prior to surgery, permitting return of some immune function, and restarted at 3–5 days after surgery in the absence of wound healing complications or infection at the surgical site or elsewhere. • There are multiple mechanisms postulated for immunosuppression with these medications, including leukopenia, interference with T cell costimulatory signaling, and blocking the de novo pathway of purine synthesis, with different time courses for onset and reversal [101,102]. • Suggest a conservative withhold of 7 days prior to surgery until additional research increases understanding of these medications.	Low
RA, SpA including AS and PsA, JIA, or SLE: Restart biologic therapy in patients for whom biologic therapy was withheld prior to undergoing THA and TKA once the wound shows evidence of healing (typically ~14 days), all sutures/staples are out, there is no significant swelling, erythema, or drainage, and there is no clinical evidence of non–surgical site infections, rather than shorter or longer periods of withholding. • The decision to restart antirheumatic therapy should be based on careful assessment of the patient's wound status and clinical judgment for absence of surgical and non–surgical site infections. Normal wound closure typically requires ~14 days.	Low
RA, SpA including AS and PsA, or SLE: Continue the current daily dose of glucocorticoids in patients who are receiving glucocorticoids for their rheumatic condition and undergoing THA or TKA, rather than administering perioperative supra-physiologic glucocorticoid doses (so-called "stress dosing"). • This recommendation specifically refers to adults with RA, AS, PsA or SLE who are receiving glucocorticoids for their rheumatic condition, and does not refer to JIA patients receiving glucocorticoids who may have received glucocorticoids during childhood developmental stages, or to patients receiving glucocorticoids to treat primary adrenal insufficiency or primary hypothalamic disease. • The literature review found information on hemodynamic instability in a systematic literature review on patients with rheumatic diseases whose mean prednisone (or equivalent) dose was ≤16 mg/day. • The CDC considers the cut-off for immunosuppression at 20 mg of prednisone/day for at least 2 weeks, and observational studies demonstrate an increase in arthroplasty infection risk with long-term steroid use >15 mg/day. • Optimization for THA and TKA should include carefully tapering the glucocorticoid dose prior to surgery to <20 mg/day, when possible [102,103].	Low

Broad recommendations

If biologic therapy is to be stopped prior to surgery, consideration should be given to stopping **3 - 5 x half-life** for the relevant drug before surgery.

Biologic therapy should not be restarted after surgery until there is good wound healing and no evidence of infection, however subtle (2), and the surgeon is happy with the wound.

For **clean surgical procedures**, (i.e. arthroscopy) washout = **3 x half life**

For **high infection risk procedures**, (i.e. GI tract surgery) washout = **5 x half life**

For bloodless procedures (such as cataract surgery) we would not advise routinely stopping biologics.

Joint Guidelines for the Management of Interruption of Biologic Therapies for Elective Surgery in Adults and Children with Rheumatoid Arthritis, JIA and Ankylosing Spondylitis

Quick reference

Drug	Dosing Regime	Low infective risk	High infective risk
Etanercept/Biosimilar	50mg s/c once weekly	1 week	2 weeks
Humira/Adalimumab	40mg s/c fortnightly	6 weeks	11 weeks
Infliximab/Biosimilar	3-5mg/kg IV 8 weekly	4 weeks	7 weeks
Rituximab/Mabthera	1g x2 IV 6-12 monthly	9 weeks	15 weeks
Tocilizumab/Roactemra	8mg/kg IV 4 weekly or 162mg s/c weekly	4 weeks	6 weeks
Certolizumab/Cimzia	200mg s/c fortnightly	6 weeks	10 weeks
Abatacept/Orencia	500mg-1000mg IV 4 wkly or 125mg s/c weekly	6 weeks	9 weeks
Golimumab/Symponi	50mg s/c once monthly	5 weeks	9 weeks
Ustekinumab/Stelara	45mg/90mg s/c every 12 weeks	10 weeks	15 weeks
Secukinumab/Cosentyx	150mg s/c once monthly	12 weeks	20 weeks

Recommence Biologics once Surgeon is happy with the wound and no other signs of infection, e.g. on antibiotics

1.Συνέχιση της θεραπείας με DMARDS (απουσία επιπλοκών!)
2.Διακοπή των bDMARDs :(μεσοδιάστημα χορήγησης)+1 εβδομάδα , πριν την επέμβαση
Rituximab:(μεσοδιάστημα χορήγησης)+1 μήνα Tofacitinib(Xeljanz):7μέρες!
3.Επανέναρξη της θεραπείας μετά από δυο εβδομάδες (απουσία επιπλοκών!)
4.Πολύ καλή ενημέρωση των ασθενών μας!!!


Ευχαριστώ πολύ!